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Emergency Care of the Thoracic Casualty . . 869
Lester W. Martin

Use of I^{131}-Labeled Protein in the Diagnosis of Pancreatic Insufficiency 877
Austin B. Chinn, Paul S. Lavik, Richard M. Stitt and G. Warren Buckaloo

Experience with a Tubeless Method of Gastric Analysis 880
Monte Malach and Benjamin M. Banks

Carcinoma Diagnosed by Examination of Pericardial Fluid 884
Melvyn Leichtling, Harry B. Reibstein, Max H. Stein and Hyman E. Bass

Medical Progress: Contributions of the Social Sciences to the Solution of Health Problems 885
Hugh R. Leavell

By the London Post 913
Correspondence 915
Nonclinical Notes 915

Medical Intelligence:
The Effects of L-Thyroxine Sodium on Nontoxic Goiter, on Myxedema and on the Thyroid Uptake of Radioactive Iodine 897
Solomon Papper, Belton A. Burrows, Sidney H. Ingbar, John H. Sisson and Joseph F. Ross

Doctors Afield: David Livingstone, Missionary, Physician and Explorer 1813–1873 899
Dana L. Farnsworth

Case Records of the Massachusetts General Hospital 901

Editorials:
Record-Breaking Half Century 911
Atomic Bomb Casualty Commission 912
Greater Boston Schools of Nursing 913
"Damsel Arise" 913

Books Received 915

Notices 916

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1. Watson, E. M., and Thompson, M. W. Am. J. Digest. Dis. *18*:326, 1951.
2. Wilson, J. L.; Root, H. F., and Marble, A.: J.A.M.A. *147*:1526 (Dec. 15) 1951.

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EMERGENCY CARE OF THE THORACIC CASUALTY

First Lieutenant Lester W. Martin, MC, USAR*

MANY excellent articles on the various phases of emergency treatment of the thoracic casualty, based on experience in World War II and Korea, have appeared in the medical literature. It seems worth while to collect and summarize the outstanding contributions that have been published, especially in these days when many young physicians are called upon to care for battle casualties. The scope of this paper is limited to emergency treatment indicated in the division area prior to admission of the casualty to a forward surgical hospital. Some of the principles outlined may also be applied to civilian practice.

Incidence

Statistics reported by Carter and DeBakey[1] indicate that chest wounds are responsible for approximately 20 per cent of the deaths on the battlefield. Chest wounds in World War II represented approximately 8 per cent of all battle casualties surviving admission to medical units.[1]

The mortality rates reported by Carter and DeBakey reveal a progressive decline, from over 60 per cent in the American Civil War to 50 per cent in World War I and to 8.1 per cent in World War II. This lowered mortality is not due to new surgical technics so much as to a better understanding of cardiopulmonary physiology, antibiotics, blood transfusions, early vigorous resuscitative measures and timing of operative intervention.[1]

Character of Wounds and Causative Agents

The character of the injury in chest wounds is an important consideration since it bears a significant relation to treatment, morbidity and mortality. The nature of the wound depends to a great extent on the type of missile producing it.

The missiles of small-arms fire generally produce small, penetrating wounds (no wound of exit) or simple, perforating wounds (with a small wound of entry and a somewhat larger exit wound). A large percentage of bullet wounds are associated with surprisingly little tissue damage and minimal cardiorespiratory disturbances. In fact, many of these simple penetrating and perforating wounds need little more than a sterile dressing, supportive measures and conservative management.[1-6]

On the other hand, fragments of high-explosive shells, bombs and mines are irregular in size and shape and travel at a high velocity without a perforating spin. They cause greater destruction of tissue, carry in fragments of bone and bits of clothing, and leave a large, irregular, dirty wound.[1, 4, 6] At a British casualty clearing station in World War II, the mortality was 10.8 per cent in 74 cases of bullet wounds, and 22.7 per cent in 216 cases of shell and shrapnel wounds.[7]

Forward Care

First-aid treatment of the thoracic casualty is initiated on the battlefield by the company aid man. Aid men are taught that sucking wounds of the chest should be closed with a large, airtight dressing, that a collapsed chest wall should be bandaged snugly and that the wounded man should be urged to cough. They are taught to transport the patient with the injured side down or in a sitting position if he has difficulty in breathing when lying down. At the battalion aid station, further treatment is given by the medical officer. Here, dressings are adjusted; petrolatum gauze may be used to occlude a sucking chest wound. Demerol may be administered or a nerve block carried out for relief of pain. A thoracentesis for removal of air or blood may be performed. A booster dose of tetanus toxoid is given, and chemotherapy (generally penicillin) is initiated. An infusion of plasma may be started and the patient given a high priority for evacuation to a clearing station and then to a forward surgical hospital. Even with a high priority for evacuation, the delay may be several hours or even days in some cases before the casualty eventually reaches an installation where operation can be performed. All along this line of evacuation the patient's treatment must be continuous.[5, 8-10]

General Diagnostic Considerations

X-ray facilities are generally not available forward of the clearing station, and the correct interpretation of physical signs becomes all important. Physical examination of the patient includes accurate localization of the external thoracic wounds and a projection of the probable course of the missile.

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By plotting the course of the missile, one can gain a general idea of the intrathoracic or thoracoabdominal damage.[10-12] This may determine the type and the urgency of operation. It may also explain failure of response to resuscitative measures and give a clue to past or future hemorrhage. Plotting of the course of the missile may be difficult or impossible in cases of perforating wounds. If there is any doubt, it is best to treat the patient as though the wound were of the thoracoabdominal type.

Careful examination of the abdomen should always be performed on thoracic casualties. Acute gastric dilatation develops in a large number of thoracic injuries, and decompression must be carried out immediately because of the limitation of diaphragmatic excursion. Abdominal pain, tenderness and spasm and a silent abdomen on auscultation may be complications of a purely thoracic wound.[8, 13] Although the decision is frequently difficult, it must be promptly determined whether these signs are due solely to intercostal-nerve damage or to intra-abdominal injury. An intercostal-nerve block may be of aid, producing cessation of the abdominal pain, tenderness and spasm. In case of peritoneal irritation, deep tenderness, and rebound tenderness generally remain after the block.[10]

Transportability

It is the duty of the medical officer in the clearing station to sort the casualties and determine whether they should be sent to the mobile army surgical hospital for immediate operation, whether they can withstand the trip farther to the rear to an evacuation hospital without more than minor emergency treatment or whether they may be returned to duty within the division.

The mobile army surgical hospital has equipment and personnel for handling only a limited number of first-priority surgical cases. When the flow of casualties is heavy, it is impossible for the small staff of doctors, nurses and enlisted men to give adequate care to all patients. It is therefore advisable that the number of patients operated on in the mobile hospital be kept at a minimum. The emphasis should be on abdominal, thoracoabdominal, traumatic amputations, vascular injuries and head injuries with increasing intracranial pressure, as well as other cases in which time lag is a major consideration.[14] It is well recognized that such casualties do not withstand the necessary delays and discomforts incident to further evacuation. Patients with thoracic injuries, on the other hand, in whom there is no possibility of diaphragmatic penetration or shock and in whom cardiorespiratory balance has been restored withstand evacuation very well. In the early campaigns of World War II it was not appreciated by many how well thoracic cases could be transported, if care was taken to assure their being in the best possible state before evacuation. Shefts,[15] working on this problem in an evacuation hospital, reported a series of 113 cases in which there was not a single death that could in any way be attributed to evacuation of the patient. Over 50 per cent of the patients with thoracic injuries seen in clearing stations during the later campaigns were evacuated directly to the evacuation hospitals. The main function of the mobile surgical hospital, so far as the majority of chest lesions is concerned, is to act as a triage center to which the medical officers at the clearing station can send any patient when they are in doubt about either his transportability or the presence of a thoracoabdominal lesion. If there is any reasonable suspicion that such an injury is present, the patient should be held in the mobile hospital for surgical exploration.

Relief of Pain

Pain from the chest wall may cause splinting of the movements of the thoracic cage, with limitation of respiratory excursions to a dangerous level. Pain may also prevent effectual cough, resulting in retention of tracheobronchial secretions and subsequent atelectasis and anoxia.

Analgesics

Morphine should be used with great caution in chest wounds.[5, 10, 16] It tends not only to depress the respiration in a patient who already has respiratory difficulty but also to depress the cough reflex and to allow the accumulation of secretions and blood in the bronchial tree.[16]

Demerol, in doses of 50 to 100 mg., is frequently valuable in relieving pain and yet does not depress the respiration and cough reflex so much as morphine. However, it causes some depression and certainly should not be used indiscriminately.

Immobilization

Pain resulting from minor rib fractures, such as those commonly seen in civilian life, can be adequately controlled by partial immobilization of the chest wall with properly applied adhesive strapping. In extensive wounds of the chest, however, strapping is often ineffectual in providing relief of pain. Also, complete immobilization of the chest by strapping may cause dangerous reduction in vital capacity.[17] Strapping, however, is of definite value for stabilization of the so-called flail chest, which exhibits paradoxical motion (discussed below in detail).

Intercostal-Nerve Block

Anesthetic block of the intercostal nerves has proved the best means of relieving thoracic pain and has been used extensively. A regional type of block is preferred to local infiltration of the injured site, because of the extent and the contamination of the wounds. When wounds are far posterior, or when regional block has not given complete relief, paravertebral injection of the same nerves is recom-

mended. By this method, the sympathetic chain, as well as the intercostal nerves, is probably infiltrated. In the performance of regional block, the injection is made at the angle of the ribs. Approximately 5 cc. of a 1 per cent solution of procaine hydrochloride is injected into each nerve, including two nerves above and two below the painful area. The resulting relief of pain is often dramatic. A patient who has been dyspneic and grunting with pain may immediately become quiet, the respirations become smooth, and the patient may often fall asleep in a few minutes.[9, 10, 18, 19] Harmon, Baker and Kornegay[20] have shown an immediate marked increase in vital capacity after procaine block; often one block suffices, but in 25 per cent of 32 cases, a second injection was required after one to four days.[20]

Paravertebral Block

For a parvertebral block, a 7.6-cm., 20-gauge (spinal-type) needle is preferred. The injection is made approximately 3 cm. from the midline. The needle is directed upward and medially until it touches the transverse process of the vertebra. The tip of the needle is then withdrawn slightly and directed below the transverse process and advanced approximately 0.5 cm.; 5 to 10 cc. of procaine is injected. As in regional block, at least two intercostal nerves above and below the lesion should be injected.

Regional block may be carried out in the battalion aid station, but paravertebral block is probably best deferred for an experienced anesthetist in one of the forward hospitals.

Anoxia

In some patients with extensive thoracic wounds a marked degree of anoxia may be present, even without the presence of cyanosis. Symptoms of anoxia consist of restlessness, apprehension, sustained rapid pulse and dyspnea. What has been described as the manic stage of restlessness has immediately preceded death in several cases.

Anoxia may be due to a combination of conditions. Reduction in vital capacity, anemia, cardiac injury and pain are all contributing factors.

Treatment consists of relief of pain by nerve blocks, administration of oxygen, blood transfusion and provision of a clear airway and complete pulmonary expansion. Cyanosis is a later manifestation of anoxia, and treatment should be instituted before it develops.[10] Under combat conditions, the only practical method of oxygen administration is generally by nasal catheter. Such a procedure must be supervised closely or else carried out by the medical officer himself, since the experience and knowledge of nonprofessional personnel can rarely be depended upon. Inadvertent insertion of the catheter into the esophagus may prove fatal.

Hemothorax

Incidence

Hemothorax of some degree can be expected in 75 to 80 per cent of all chest wounds.[1, 21] Generally the bleeding is from the chest wall (intercostal or internal mammary vessels).[17] Occasionally, bleeding results from the lung itself, but this generally ceases promptly. Injury to the hilar structures usually results in immediate death on the battlefield.[1]

General Management

The management of hemothorax was the subject of considerable controversy in the earlier war literature. At present, however, the treatment is well defined, and based on a thorough understanding of cardiorespiratory physiology. The following ill effects of even a minimal hemothorax should be borne in mind:

Blood in the thoracic cavity forms an ideal culture medium for bacteria, with resulting empyema.[13]

Organized hemothorax produces a fibrothorax, with fixation of that side of the chest. The subsequent deformity with its disturbed respiratory physiology is a well known entity.[22-24]

Hemothorax is never completely absorbed, and thus the lung is prevented from complete expansion.

It is now generally agreed among military surgeons[19, 25-30] that hemothorax should be completely aspirated as soon as possible, with repetition at frequent intervals, thus achieving early pulmonary expansion. Also, infection and organization of the clot are avoided.

Volume of Blood Removed

The quantity of blood that should be removed at each aspiration has been a subject of considerable discussion. During the Algerian and Tunisian campaigns, each thoracentesis was limited to 400 to 600 cc. Since there were no ill effects, 600 to 800 cc. was removed at each tap in the Sicilian campaign. Again, no adverse results were observed, and this led to the practice, during the French and Belgian campaigns, of aspirating the chest as much as possible each time. The procedure was well tolerated by all patients, the number of aspirations was reduced, early re-expansion was favored, and the incidence of clotting in the hemothorax was undoubtedly reduced. There were no sudden deaths at any time as a result of the aspiration. The most common untoward effect was pain in the shoulder of the affected side. This usually subsided after a few hours. An occasional patient complained of tightness in the chest, which also always subsided after a few hours without any specific treatment.[31]

Theory of Air Replacement

Air replacement has been advocated. It is mentioned here only to be condemned. The theory in favor of it was that the replaced air would tend to prevent a pressure differential between the vessels and the pleural space, with resulting renewed bleeding. It should be recalled that the bleeding is generally from the intercostal vessels and not from the lung. Also, the pressure in the pulmonary circulation is extremely low anyway. Air replacement actually prevents re-expansion of the lung and should not be employed.[32-35]

Technic of Thoracentesis

Thoracentesis for hemothorax is carried out with a needle of 15 to 17 gauge connected through a three-way stopcock to a 30-cc. syringe. The needle may be introduced through the eighth or ninth interspace posteriorly or laterally. Use of the three-way stopcock prevents aspiration of air while the syringe is being emptied. At the completion of aspiration, the instillation of 300,000 units of crystalline penicillin and 1 gm. of streptomycin into the pleural cavity is considered a good procedure by most authorities.[5]

Thoracotomy

As pointed out by Valle,[5] closed thoracotomy with catheter drainage attached to the underwater seal is undesirable for treatment of simple hemothorax in forward areas. This procedure results in a higher incidence of empyema. Closed drainage for hemothorax usually loses its value within twenty-four to forty-eight hours because of occlusion of the tube by fibrin and clots and by pleural adhesions about the intrathoracic portion of the tube. Also, should thoracentesis be necessary after removal of the tube, it is more difficult because of fluid loculations resulting from adhesions produced by the tube. Experience has shown that two or three thoracenteses require less time than a closed thoracotomy with insertion of an intercostal tube, so that the time factor favors thoracentesis. Lastly, a thoracotomy tube with underwater drainage requires more expert care in transit. Inexperienced personnel cannot be entrusted with such an apparatus.

Thoracentesis should be carried out every day so long as blood accumulates. Open thoracotomy for hemothorax should be reserved for the few cases of uncontrolled bleeding in which the hemothorax reaccumulates rapidly after repeated aspirations.[5, 14, 35]

Streptokinase and Streptodornase

The use of streptokinase and streptodornase in hemothorax has been a topic of considerable recent discussion.[36] It is available in most overseas hospitals[35] and no doubt is of some value in old clotted hemothorax. It probably should not be used, however, before approximately ten days after the bleeding has ceased. It is thought to cause renewed bleeding in fresh cases. Its use, therefore, is not indicated for hemothorax in the division area.

Open Pneumothorax (Sucking Wounds)

Airtight Dressings

The extreme emergency of a sucking chest wound and the necessity for immediate airtight closure are well understood.[2, 19, 29, 32, 37-40] The company aid men should all be thoroughly instructed in this matter, since what is done during the first few minutes may mean life or death for the patient. At the battalion aid station adequate closure should be accomplished by application of large strips of petrolatum gauze bridged over the open wound and a large gauze pad secured in place over it by tightly applied, wide strips of adhesive plaster, an airtight closure being thus assured. Surgical closure at division-area installations should not be carried out. Adequate closure cannot be obtained. In cases in which forward surgical closure was attempted in World War II, the skin was generally used to make the wound airtight. The resulting subcutaneous emphysema frequently extended from the forehead to the scrotum. Also, some patients who have had such closures have suffered tension pneumothorax and died on the way to the hospital.[32]

Frequently, death results during transit of a casualty because of failure to recognize and close an open chest wound. Past experience has revealed a number of cases of apparently simple wounds of the chest wall, with no suggestion of an open wound, in which, when the patient produced a forceful cough, a column of blood projected from the wound. An open pneumothorax was thus demonstrated. Occasionally, the sucking nature of a chest wound is demonstrated only when the patient's arm is placed in a certain position. A good policy is to apply an airtight dressing to all chest wounds.

Thoracentesis

After airtight closure of a sucking chest wound, the pneumothorax should be aspirated to allow full expansion of the lung. Also, if the patient performs a Valsalva maneuver (forced expiration on a closed glottis) just prior to application of the airtight dressing, most of the pneumothorax may be expelled. A tension pneumothorax develops only rarely in such a case, but it occasionally does, and the possibility should be borne in mind. It should be treated the same as any other tension pneumothorax.

Tension Pneumothorax

Etiology

Tension pneumothorax may develop as a complication of penetrating or perforating wounds of the chest.[10, 41] When it does occur, it constitutes a true emergency. It is generally caused by a laceration of the lung or bronchus that acts as a ball valve. It occasionally results from a sucking wound

of the thoracic wall. In either event, air is sucked into the pleural cavity with each inspiration but cannot escape.[19, 29] Under such conditions the intrapleural pressure steadily rises and may be rapidly fatal unless corrective measures are taken immediately.

Diagnosis

The diagnosis is at times difficult even though the possibility is kept in mind. The critical condition of the patient alone may make a detailed examination difficult. When one is confronted with a seriously wounded soldier, with the limited facilities of a battalion aid station, possibly in sub-zero weather, and a heavy load of casualties awaiting life-saving measures, tension pneumothorax may be easily overlooked. The extreme dyspnea, cyanosis, tracheal deviation, tense accessory muscles of respiration, a bulging, fixed chest and hyperresonance to percussion should leave no doubt about the diagnosis.

Treatment

The treatment is simple, and the results dramatic. A needle of fairly large caliber (15 to 16 gauge) should be inserted into the chest anteriorly through the second interspace in the mid-clavicular line.[5, 42] This allows excess air to escape. For continued decompression in the valvular type of case, a flutter valve may be attached to the end of the needle. Hospital management usually employs closed drainage (attached to underwater drainage). During transportation, however, this is not feasible, and a satisfactory flutter valve may be devised by the passing of a 15-gauge needle through a rubber stopper of a saline bottle and insertion of the needle into the chest. The stopper is then firmly strapped to the chest wall with adhesive tape. One may easily fashion a flutter valve by cutting the end off a finger cot or condom and attaching it to the end of the needle. Response to this management is immediate and effective: a patient who has been fighting for breath will suddenly resume calm respirations and is soon resting comfortably. Such decompression can usually be discontinued within twenty-four to forty-eight hours, except in some of the valvular types, in which it must be continued as long as a week.

Mediastinal Emphysema

Mediastinal emphysema may result from a penetrating or crushing injury with a tear of the esophagus, trachea or a large bronchus and the escape of air into the mediastinum.[42, 43] Theoretically, this may produce serious compression of the mediastinal structures, with resultant dysphagia, circulatory failure, obstruction of the trachea, cyanosis and eventually death.[42]

In 1364 thoracic injuries seen by the Second Auxiliary Group in World War II,[14] mediastinal emphysema per se was never a problem, not being under enough pressure to obstruct venous return to the heart and to become symptomatic. It is suggested that many of the symptoms commonly ascribed in the literature to mediastinal emphysema have been due to unrecognized accompanying pressure pneumothorax.[14]

Subcutaneous Emphysema

Subcutaneous emphysema may result from a laceration of the lung and parietal pleura that allows the air from the bronchial passages to escape into the subcutaneous tissue.[42]

Subcutaneous emphysema may become extensive but generally requires no specific therapy.[22, 42] Its importance lies in its indication that an underlying pneumothorax may be present. The pneumothorax should be treated by aspiration or drainage, as outlined above.

Crushed Chest

The so-called "stove-in" (crushed) chest is a term applied to a fracture of several adjacent ribs in two or more places, and characterized by paradoxical movement of the fragments during respiration. The condition generally results from blunt injury to the chest wall. The patient may exhibit marked dyspnea and rapidly become cyanotic. Respirations become rapid and labored. The blood pressure may fall rapidly, and a picture of severe anoxia supervenes; the cough mechanism is impaired or completely absent. The patient soon becomes exhausted, and the cough is ineffective in clearing the bronchial tree of accumulating secretions.[10]

Treatment consists of immobilization of the chest wall and relief of the pain. The chest wall may be immobilized with dressings and adhesive strappings.[8] Incorporation of several tongue depressors in the strapping frequently aids immobilization. It is essential that the adhesive strapping be applied from midline to midline, and that it extend well above and well below the lesion. The use of small sand bags may be of value in immobilizing the chest wall. Proper positioning of the patient with the injured side down is also important.[10]

In certain cases of crushing injury to the anterior portion of the chest, such as that commonly sustained by the driver in an automobile accident, skeletal traction may be necessary to provide immobilization of the paradoxical segment.[17, 44] This would be difficult in combat, but some type of support might be improvised similar to the ladder used by Lester[45] for support of the sternum in the postoperative management of cases of funnel chest. Intercostal-nerve block is frequently indicated for relief of pain. Associated complications of hemothorax, pneumothorax and traumatic "wet lung" are often present and should be treated according to the principles outlined for each.

Traumatic Wet Lung

General Considerations

The syndrome of excessive accumulation of secretions and blood in the tracheobronchial tree occurring a few hours up to seven days after injury to the chest has been referred to as "wet lung."[10, 21] It is a complication of thoracic trauma that commonly follows pulmonary blast injuries, fractured ribs and any blunt injury to the chest. It occasionally occurs after intrathoracic wounds and wounds of the chest wall.[10, 21, 46]

During the immediate post-traumatic period, the complications may be serious and, if untreated, may result in death. Its presence always increases the surgical risk, and, if possible, general anesthesia should be avoided during the acute stage.

Mechanism

As pointed out by Burford and Burbank,[46] the lung reacts to trauma just as uniquely as the brain or any highly specialized organ. This fundamental response consists of an increased fluid production and retention of that fluid in the bronchopulmonary system. The exact mechanism is not clearly understood. Brewer et al.[21] point out two groups of factors that are responsible for wet lung: those leading to excess production of bronchial fluids, and those preventing adequate removal of the fluid. Under the former they include the effect of intrabronchial hemorrhage, or blood entering the bronchial tree from hemothorax through a bronchopleural fistula, secretions from the upper respiratory tract as the result of infections and, what is probably more important, reflex bronchial spasm with excess bronchial secretions. That bronchospasm with excess secretions is a reflex phenomenon was demonstrated in animal experiments by de Takats.[47] The exact mechanism, however, is still not clear. Bronchoconstrictor fibers are derived from the vagus.[48] Yet Daniel and Cate[49] have shown increased susceptibility of animals to pulmonary edema after bilateral vagotomy. Dorsal sympathecotomy reduces the incidence. Atropine is of little or no value in the treatment or prevention of wet lung.[21]

The second group of factors, or those inhibiting removal of the fluid, includes obstruction of the bronchial tree with exudate, mucus and blood[50]; depression of the cough reflex from oversedation with opiates; unconsciousness; flail chest, with paradoxical motion; and chest-wall pain preventing effectual cough.

Diagnosis

The symptoms consist of moderate to severe shock, hemoptysis, chest pain, restlessness and a frequent "wet," painful cough. The cough is noneffectual in that only small amounts of sputum are raised and the bubbling character of the respirations persists. The common physical findings are moderate cyanosis, dyspnea, orthopnea and impaired resonance to dullness on percussion in scattered areas varying up to an entire lobe in size, over which breath sounds are markedly diminished and bronchovesicular. Blood and tenacious mucus form the bulk of the obstructing fluid, small amounts of which may be coughed up. Acute, massive collapse of the lung and death occasionally result from occlusion of a main bronchus.

Treatment

The logical therapy consists of abolition of pain, physiologic remobilization of the chest wall and clearing the tracheobronchial tree. Procaine block of the intercostal nerves, as advocated by Burford and Burbank,[46] frequently has dramatic results. The patient is immediately relieved of pain, the chest wall is no longer splinted, and the cough becomes productive. The intercostal-nerve block probably acts not only to relieve the pain but also to interrupt the reflex arc responsible for bronchospasm and excess secretions.[21, 47]

If the patient is unable to cough effectively because of physical exhaustion, or if secretions continue to flood the bronchi, mechanical suction should be resorted to without delay. Either tracheobronchial aspiration by catheter or bronchoscopy may be employed. The former is a more valuable procedure in the division area since no special materials are required. The technic is simple, and no anesthesia is needed. An ordinary small urethral catheter may be connected with infusion tubing to the windshield-wiper attachment of a motor vehicle, which provides adequate suction under combat conditions. Suction, which may be necessary at hourly intervals, should be carried out whenever the secretions reaccumulate. The catheter should be introduced into the nose and directed posteriorly until it can be felt to touch the arytenoid cartilage. This usually stimulates a cough reflex. The catheter may then be advanced quickly into the trachea simultaneously with the expiratory phase of the cough or during the deep inspiration that follows it. Suction is ordinarily not turned on until after the catheter has been inserted into the trachea unless the suction is necessary to stimulate the cough reflex.[51] After the trachea has been cleared by repeated short bursts (five to ten seconds) of intermittent suction, the main bronchi may be cleared in the same way by turning of the patient from side to side. This procedure not only aspirates considerable material but also stimulates the patient to cough up copious amounts.

Bronchoscopy is undoubtedly more efficient but requires the services of experienced personnel, special equipment, local anesthesia and facilities more elaborate than those available in the division area. Oxygen therapy should be administered as far forward as possible.[21] Fluids should be used judiciously, being administered slowly and limited

to 1500 to 2000 cc. per twenty-four hours. Paravertebral procaine blocks have been recommended and appear to be of value in some cases.[10, 46] Atropine has been found to be of little or no value clinically.[21, 47]

When the patient is comatose or unresponsive, tracheal aspirations may be required at frequent intervals. It is often convenient to leave the intratracheal catheter in place and to use it for aspiration of fluid material when necessary and for the administration of oxygen between aspirations. Caution should be exercised to assure the correct position of the catheter.

Thoracoabdominal Wounds

All chest wounds should be examined with the possibility of a thoracoabdominal wound in mind. A thoracoabdominal wound is defined as one in which the missile has penetrated both the thoracic and abdominal cavities by traversing the diaphragm.

Any casualty with the wound of entrance below the fourth interspace anteriorly or below the seventh rib posteriorly should be managed as a thoracoabdominal injury and given the highest of priorities for evacuation and early operative intervention.[52, 53] This is especially true if the wound is on the left side, since in such cases injuries to the colon, stomach and spleen are frequent. Plotting of the course of the missile or, in the event of penetrating wounds, inquiry of position when the injury occurred, may be of considerable value. The time lag in thoracoabdominal injuries is as important as or more important than in abdominal injuries. Every casualty with a thoracoabdominal wound, or any question of diaphragmatic penetration, should be sent directly to a mobile surgical hospital for immediate surgical exploration.[5, 14, 35, 53]

Heart Injuries

General

Among 2267 consecutive thoracic wounds in World War II, there were 75 wounds involving the heart or pericardium[14] (an incidence of 3.3 per cent). In the division area treatment is limited to general supportive measures. No special measures are indicated except in cases of cardiac tamponade.

Cardiac Tamponade

Cardiac tamponade was a rare finding in battle casualties in World War II,[14] as compared to the frequency in civilian life. However, when it does occur, immediate measures are necessary or death will soon result. The pericardium is an inelastic structure. With the accumulation of 200 to 250 cc. of blood in the pericardial sac, the intrapericardial pressure soon becomes equal to the effective venous pressure, resulting in circulatory failure and death.

The clinical picture of circulatory failure from cardiac tamponade is well known and consists of a fall in systemic blood pressure, elevated venous pressure (distended neck veins and so forth) a thready pulse and distant or absent heart sounds. If x-ray facilities are available, an enlarged cardiac shadow, with the typical "water-bottle" appearance, and decreased pulsation as seen on fluoroscopy are of great aid in establishing a diagnosis.

Treatment is directed at relieving the pressure, stopping the bleeding and replacement of blood. The limited facilities in the forward area pose many restrictions on treatment, which is limited to life-saving measures, and evacuation is carried out as soon as possible. Therefore, in cardiac tamponade, the emergency treatment consists of general supportive measures in addition to relief of the intrapericardial pressure by pericardicentesis. This is more safely done by the left costoxiphoid route, which entails less danger of injury to the heart wall, and especially of one of the coronary arteries. It also avoids possible injury to the internal mammary vessels, with resultant hemorrhage.[14, 35]

The patient should be evacuated as soon as possible to a mobile surgical hospital, where further operative measures may be carried out as indicated.

Summary and Conclusions

The majority of chest injuries can be effectively treated under combat conditions with limited facilities if medical officers are acquainted with the problems encountered. The indications for emergency operative thoracotomy are as follows: continuing, rapidly accumulating intrathoracic hemorrhage despite repeated thoracenteses (hemothorax alone is not an indication for thoracotomy); any likelihood of diaphragmatic penetration from the wound; evidence of damage to the mediastinal viscera (esophagus or trachea); wounds of large bronchi or rapidly accumulating tension pneumothorax not controlled by more conservative methods; large intrapleural foreign bodies readily accessible by extension of the wound; and cardiac injuries.

Patients in these groups should be sent to the nearest surgical hospital for operative intervention. Other patients withstand transportation quite well and may be evacuated in the normal chain of evacuation if treated in accordance with the principles outlined.

Hemothorax should be treated by early and complete thoracentesis, repeated as indicated.

Emergency treatment of an open pneumothorax is limited to the application of an airtight dressing, after which the patient will generally withstand transportation.

Tension pneumothorax is most adequately treated in combat by insertion of a large needle anteriorly followed by attachment of an improvised flutter valve. (For hospital treatment, a closed thoracotomy tube attached to underwater suction is undoubtedly more satisfactory.)

Mediastinal emphysema and subcutaneous emphysema per se rarely threaten the life of a patient. Their greater importance lies in their indication of a possible underlying pneumothorax.

The "stove-in" (crushed) chest requires immobilization of the paradoxical segment of chest wall.

Traumatic "wet lung" is best treated by intercostal-nerve block for relief of pain and tracheal-catheter or bronchoscopic aspiration of accumulated secretions.

Cardiac tamponade is more safely aspirated by the costoxiphoid route.

References

1. Carter, B. N., and DeBakey, M.E. Current observations on war wounds of chest. *J. Thoracic Surg.* **13**:271-293, 1944.
2. Holman, E. Experiences with chest wounds from Pacific combat area. *Ann. Surg.* **119**:1-25, 1944.
3. Overton, M. C., Jr., and Criss, R. J., Jr. Perforating wounds of chest. *U. S. Nav. M. Bull.* **42**:1021-1024, 1944.
4. Puckett, W. O., McElroy, W. D., and Harvey, E. N. Studies on wounds of abdomen and thorax produced by high velocity missiles. *Mil. Surgeon* **98**:427-439, 1946.
5. Valle, A. R. Emergency treatment of chest injuries. The Surgeons Circular Letter, GHQ, FEC. Symposium on Military Medicine in the Far East Command, 1951.
6. Callender, G. R. Wound ballistics. *War Med.* **3**:337-350, 1943.
7. Cask, G. E., and Wilkinson, K. D. Penetrating gunshot wounds of chest and their treatment. *Brit. M. J.* **2**:781-786, 1917.
8. Rogers, W. L., and Holman, E. Care of thoracic wounds as adapted to Pacific theater. *U. S. Nav. M. Bull.* **45**:711-716, 1945.
9. Sanger, P. W. Evacuation hospital experiences with war wounds and injuries of chest: preliminary report. *Ann. Surg.* **122**:147-162, 1945.
10. Samson, P. C., Burbank, B., Brewer, L. A., III, and Burford, T. H. Immediate care of wounded thorax. *J. A. M. A.* **129**:606-610, 1945.
11. Betts, R. H. Initial surgery of thoracoabdominal war injuries. *J. Thoracic Surg.* **15**:349-364, 1946.
12. Mackler, S. A. Experience with thoracic and thoracoabdominal wounds in evacuation hospital. *J. Thoracic Surg.* **16**:538-570, 1947.
13. Burford, T. H., Parker, E. E., and Samson, P. C. Early pulmonary decortication in treatment of post-traumatic empyema. *Ann. Surg.* **122**:163-150, 1945.
14. Forsee, J. H. Unpublished data.
15. Shefts, L. M., Doud, E. A., Sandzen, S. C., Rose, W. F., and Michels, L. M. Unpublished data.
16. Beecher, H. K. *Resuscitation and Anesthesia for Wounded Men: The management of traumatic shock.* 161 pp. Springfield, Illinois: Charles C Thomas, 1949.
17. Blades, B. Physiologic principles underlying treatment of injuries to chest. *Am. J. Surg.* **78**:665-667, 1949.
18. Fitzpatrick, L. J., and Adams, A. J. Nerve block in treatment of thoracic injuries. *J. Thoracic Surg.* **14**:480-483, 1945.
19. Blades, B. Emergencies of injuries of chest. *J. A. M. A.* **135**:812-814, 1947.
20. Harmon, P. H., Baker, D. R., and Kornegay, R. D. Uncomplicated fractures of ribs and major injuries of chest wall: treatment by infiltration with local anesthetic. *J. A. M. A.* **118**:30-34, 1942.
21. Brewer, L. A., III, Burbank, B., Samson, P. C., and Schiff, C. A. "Wet lung" in war casualties. *Ann. Surg.* **123**:343-362, 1946.
22. Johnson, J. Battle wounds of thoracic cavity. *Ann. Surg.* **123**:321-342, 1946.
23. Harken, D. E. Review of activities of thoracic center for III and IV hospital groups, 160th General Hospital, European Theater of Operations, June 10, 1944 to Jan. 1, 1945. *J. Thoracic Surg.* **15**: 31-43, 1946.
24. Cameron, D. A., O'Rouke, P. V., and Burt, C. W. Management of penetrating and perforating wounds of chest in civilian practice. *Am. J. Surg.* **79**:361-368, 1950.
25. Churchill, E. D. Trends and practices in thoracic surgery in Mediterranean theater. *J. Thoracic Surg.* **13**:307-315, 1944.
26. Gardner, C. E., Jr. Chest injuries: symposium on aseptic surgical technic and its application to thoracic surgery; application of military experience to civilian practice. *S. Clin. North America* **26**:1082-1094, 1946.
27. O'Neill, J. N. Diagnosis and surgical management of thoracoabdominal wounds aboard assault transport. *U. S. Nav. M. Bull.* **46**: 1724-1728, 1946.
28. Brodkin, H. A. Traumatic hemothorax. *Am. J. Surg.* **72**:569-572, 1946.
29. Moore, R. L. War injuries of chest. *Ann. Surg.* **124**:367-382, 1946.
30. Iovine, V. M. Treatment of penetrating and perforating chest wounds: discussion of its complication, organized hemothorax. *Am. J. Surg.* **78**:677-683, 1949.
31. Snyder, J. M., and Tropea, F., Jr. War injuries of chest: report of series of 678 cases. *Surgery* **22**:780-800, 1947.
32. Snyder, H. E. Management of intrathoracic and thoracoabdominal wounds in combat zone. *Ann. Surg.* **122**:333-357, 1945.
33. Kent, E. M., and Tebrock, H. E. Post-traumatic hemothorax management. *U. S. Nav. M. Bull.* **45**:14-21, 1945.
34. Betts, R. H., and Lees, W. M. Military thoracic surgery in forward area. *J. Thoracic Surg.* **15**:44-63, 1946.
35. *Management of Batile Casualties (TB Med. 147).* 29 pp. Washington, D. C.: Government Printing Office, June 22, 1951. Par. 12.
36. Tillet, W. S., Sherry, S., Christenson, L. R., Johnson, A. J., and Hazelhurst, G. Streptococcal enzymatic debridement. *Ann. Surg.* **131**: 12-22, 1950.
37. Meade, R. H. Discussion of Ferguson, L. K., and Brown, R. B. Injuries of thorax in battle casualties. *Am. Rev. Tuberc.* **50**:293-304, 1944.
38. Welch, C. S., and Tuhy, J. E. Sucking wounds of chest. *Surg., Gynec. & Obst.* **81**:183-191, 1945.
39. Blau, M. H. Emergency treatment of chest wounds. *South. M. J.* **42**: 851-855, 1949.
40. Miscall, L. Thoracic injuries. *S. Clin. North America* **30**:397-404, 1950.
41. Watson, G. S. Traumatic valvular pneumothorax. *Brit. M. J.* **2**: 693, 1947.
42. Ritter, H. H., and Kaye, B. B. Trauma of thorax: collective review. *Am. J. Surg.* **64**:191-208, 1944.
43. Cowart, J. T. Mediastinal emphysema: report of 2 cases. *U. S. Nav. M. Bull.* **43**:119-121, 1944.
44. Williams, M. H. Severe crushing injuries to chest: report of case having extensive bilateral rib fractures successfully treated by pericostal skeletal traction. *Ann. Surg.* **128**:1006-1011, 1948.
45. Lester, C. W. Funnel chest and allied deformities of thoracic cage. *J. Thoracic Surg.* **19**:507-522, 1950.
46. Burford, T. H., and Burbank, B. Traumatic wet lung: observations on certain physiologic fundamentals of thoracic trauma. *J. Thoracic Surg.* **14**:415-424, 1945.
47. DeTakats, G., Fenn, G. K., and Jenkinson, E. L. Reflex pulmonary atelectasis. *J. A. M. A.* **120**:686-690, 1942.
48. Best, C. H., and Taylor, N. B. *Physiological Basis of Medical Practice.* Fifth edition. 1330 pp. Baltimore: Williams and Wilkins, 1950.
49. Daniel, R. A., Jr., and Cate, W. R., Jr. "Wet lung": experimental study. *Ann. Surg.* **127**:836-857, 1948.
50. Drinker, C. K., and Warren, M. F. Genesis and resolution of pulmonary transudates and exudates. *J. A. M. A.* **122**:269-273, 1943.
51. Haight, C. Intratracheal suction in management of post-operative pulmonary complications. *Ann. Surg.* **107**:218-228, 1938.
52. Welch, C. S., and Tuhy, J. E. Combined injuries of thorax and abdomen. *Ann. Surg.* **122**:358-374, 1945.
53. Betts, R. H. Thoraco-abdominal injuries: report of twenty-nine operated cases. *Ann. Surg.* **122**:793-806, 1945.

Additional References

Adams, H. D. Thoracic casualties from Marianas. *U. S. Nav. M. Bull.* **44**:1234-1238, 1945.

Alexander, J. Thoracic injuries. *Am. J. Surg.* **67**:360-369, 1945.

Blades, B., and Dugan, D. J. War wounds of chest observed at Thoracic Surgery Center, Walter Reed General Hospital. *J. Thoracic Surg.* **13**:294 and 306, 1944.

Blades, B. Recent observations concerning treatment of chest wounds. *S. Clin. North America* **24**:1410-1423, 1944.

Bolman, R. M., and Caul, C. J. Thoraco-abdominal wounds without abdominal signs: report of 2 cases. *Ann. Surg.* **123**:992-998, 1946.

Brown, R. B., and Boyd, S. A. Thoracotomy versus thoracentesis: for initial drainage of traumatic hemothorax and hemopneumothorax. *U. S. Armed Forces M. J.* **3**:557-560, 1952.

Burbank, C. B., Falor, W. H., and Jones, H. W., Jr. Three hundred seventy-four acute war wounds of thorax. *Surgery* **21**:730-738, 1946.

Burke, J., and Jacobs, T. T. Penetrating wounds of chest. *Ann. Surg.* **123**:363-376, 1946.

Cuono, J. D. Paradoxical respiration. *U. S. Nav. M. Bull.* **42**:136-139, 1944.

Idem. Traumatic hemothorax. *U. S. Nav. M. Bull.* **43**:1107-1110, 1945.

Idem. Comments on casualties aboard assault cargo vessel: with report of 2 thoracic cases. *U. S. Nav. M. Bull.* **44**:1273-1276, 1945.

Eaton, R. M. Pulmonary edema. *J. Thoracic Surg.* **16**:668-694, 1947.

Forsee, J. H. Use and control of thoracic surgical teams of auxillary surgical group. *J. Thoracic Surg.* **14**:425-433, 1945.

Fox, D. B. Thoracoabdominal wounds: review of 270 cases. *Surg., Gynec. & Obst.* **82**:64-70, 1946.

Hoopes, B. F., and Propp, S. Nonpenetrating gunshot wound of chest with extensive pulmonary hemorrhage: case report with autopsy. *U. S. Nav. M. Bull.* **45**:531-536, 1945.

Kay, E. B., and Meade, R. J., Jr. War injuries of chest. *Surg., Gynec. & Obst.* **82**:13-24, 1946.

Larson, E. E. Gunshot. *Am. J. Surg.* **72**:869-874, 1946.

Merrill, A. J., Warren, J. V., Stead, E. A., and Brannon, E. S. Circulation in penetrating wounds of chest: study by method of right heart catheterization. *Am. Heart J.* **31**:413-417, 1946.

Martin, J. D., Jr. War wounds of chest. *Surgery* **21**:381-389, 1947.

Miscall, L., and Harrison, A. W. Thoracic surgery in hospital center. *Ann. Surg.* **125**:142-156 and 311-333, 1947.

Montgomery, H., Halbersleben, D., and Carr, F. B. Puncture wounds of chest. *J. Thoracic Surg.* **16**:407-415, 1947.

Paine, J. R., and Plankers, A. G. Review of patients with intrathoracic disease and injury treated on surgical service of United States Army general hospital in North Africa. *Surgery* **18**:401-411, 1945.

Robertson, R. Crushing injuries of chest. *J. Thoracic Surg.* **15**:324-335, 1946.

Rogers, W. L., and Holman, E. Penetrating wounds of chest in Pacific area: analysis of 180 cases. *Ann. Surg.* **124**:1076-1081, 1946.

Samson, P. C., and Brewer, L. A., III. Principles of improving inadequate tracheobronchial drainage following trauma to chest: further problems in treatment of wet lung. *J. Thoracic Surg.* **15**:162-172, 1946.

Samson, P. C., and Burford, T. H. Management of thoracic wounds in overseas theater. *Bull. U. S. Army M. Dept.* **6**:711-728, 1946.

Shefts, L. M., and Dowd, E. A. Management of thoracic and thoracoabdominal wounds in forward areas in Sicilian and Italian campaigns. *J. Thoracic Surg.* **15**:205-223, 1946.

Stickney, J. M., and Hagedon, A. B. Chest injuries and traumatic asphyxia. *Proc. Staff Meet., Mayo Clin.* **19**:207-213, 1944.

Tuttle, W. M., Langston, H. T., and Crowley, R. T. Treatment of intrathoracic wounds. *Surg., Gynec. & Obst.* **81**:158-168, 1945.

Valle, A. R., and Watkins, D. R. Experience in treatment of chest wounds in general hospital. The Surgeons Circular Letter, GHQ, FEC. Symposium on Military Medicine in the Far East Command, 1951.

Welch, C. S., and Tuhy, J. E. Thoracic surgery in forward areas. *Am. J. Surg.* **71**:587-598, 1946.

West, J. P. Chest wounds in battle casualties. *Ann. Surg.* **121**:833-839, 1945.

Idem. Chest wounds in battle casualties. *Ann. Surg.* **123**:986-991, 1946.

Williams, M. H. Intrabronchial hemorrhage in battle casualties. *J. Thoracic Surg.* **16**:342-352, 1947.

Wylie, R. H., Hoffman, H. L., Williams, D. B., and Rose, W. F. Thoracoabdominal casualty. *Ann. Surg.* **124**:463-478, 1946.

USE OF I^{131}-LABELED PROTEIN IN THE DIAGNOSIS OF PANCREATIC INSUFFICIENCY*

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CHRONIC pancreatic insufficiency characteristically results in faulty digestion of fat and protein, with excessive loss of free fat and nitrogen in the stool. Accurate appraisal of the degree of fat and nitrogen loss necessitates metabolic-balance studies in which the amount ingested is compared with that excreted in the feces. The over-all problems connected with such observations make them too laborious and difficult to carry out in the hospital's general wards.

Lavik and Miller[1] have recently described experiments in dogs before and after pancreatectomy using a meal of I^{131}-labeled protein. They observed that the rise in radioactivity in the blood after feeding of the test meal was distinctly retarded after pancreatectomy. Such an effect would be in keeping with a diminished hydrolysis of protein in the intestine because of pancreatic insufficiency. Furthermore, it was shown[2] that I^{131}-labeled protein was completely hydrolyzed by the digestive enzymes of dogs without splitting off more than 5 to 10 per cent of the isotope as inorganic iodide. Since a large proportion of the I^{131} remains bound to either the protein or its hydrolytic products (such as I^{131}-labeled tyrosine), the isotope may be used to follow the process of protein digestion and absorption. This report concerns observations made after the administration of a test meal of I^{131}-labeled protein to 11 persons without gastrointestinal disease and to 5 patients with chronic pancreatic insufficiency.

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METHODS

The procedure used in the preparation of the I^{131}-labeled casein‖ was similar to that described by Fine and Seligman.[3] By the use of radioactive iodine** of fairly high specific activity, the tyrosine in the protein molecule can be adequately "tagged" with the isotope without the introduction of enough iodine to alter significantly the properties of the protein.[4] The test meal was prepared immediately before use by careful mixing of the following in a Waring Blendor operating at low speed: 500 to 600 cc. of distilled water and, for each kilogram of body weight of the patient, 1 gm. of casein and 2 microcuries of I^{131}-labeled casein.

The isotope content of the individual urine and fecal samples was determined most conveniently with a scintillation counter[5] as described elsewhere.[2] The samples required no special preparation for this method of counting, except that the fecal specimens were thoroughly blended with a motor-driven stirrer to ensure a uniform distribution of isotope within the sample. When oxalated blood samples were drawn, each was assayed for I^{131} with an end window counter after being dried in the presence of alkaline silver nitrate.

The procedure employed in the study of the digestion and absorption of protein in the patients was as follows: to prevent the accumulation of I^{131} in the thyroid gland, 45 minims of Lugol's solution was given orally to each patient daily for two to three days before the test meal. On the first morning of each test period breakfast was omitted, and the test meal taken directly from the Blendor jar by means of a glass tube. The total of I^{131} consumed was readily calculated from the known amount of labeled protein present in the test meal minus that recovered in the glass tube and Blendor jar. During

‖Casec, available from Mead Johnson and Company, Evansville, Indiana.

**Obtained on allocation from the Isotope Division of the United States Atomic Energy Commission.

the next seventy-two hours individual stool specimens were collected in glass jars containing 200 cc. of half-normal solution of sodium hydroxide, and the urine specimens in glass bottles containing about 3 gm. of sodium hydroxide. Venous-blood samples were drawn from some of the patients at intervals during the first three hours after the administration of the test meal. The isotope content of the fecal, urine and blood samples was determined, and the results expressed as percentage of the ingested I^{131}.

Eleven persons without gastrointestinal disease were selected from the hospital population. The and throughout the second study period, pancreatic extract was administered with all meals, including the test meal. In all study periods the patients received the regular hospital diet except on the morning when the labeled protein was given.

Results

Results of urinary and fecal excretion of I^{131} in the 11 persons without gastrointestinal disease and 5 persons with pancreatic insufficiency are given in Tables 1 and 2 and Figures 1 and 2. In the control group, urinary excretions for seventy-two hours

Table 1. *Fecal and Urinary Excretion of Isotope after a Test Meal of I^{131}-Labeled Casein in Patients without Disease of the Gastrointestinal Tract.*

Patient	Age	Weight	Hospital No.	Diagnosis	I^{131} Excretion (Percentage Ingested)					
					Urine					Feces
	yr.	*kg.*			*6 hr.*	*12 hr.*	*24 hr.*	*48 hr.*	*72 hr.*	*72 hr.*
G. Q.	14	64.6	615453	Chronic lung disease of unknown etiology	9.0	46.7	60.4	85.6	90.1	0.9
M. M.	67	58.9	613621	Laënnec's cirrhosis	6.4	21.0	42.0	62.0	70.0	2.4
L. A.	14	49.3	197616	Epilepsy	4.6	45.5	59.3	75.4	78.5	1.5
L. F.	41	73.0	294028	Leg ulcer	19.9	44.0	54.0	69.0	74.3	4.8
P. G.	60	66.4	294716	Infectious arthritis	23.0	35.4	47.8	62.4	66.1	2.7
E. A.	46	70.4	616148	Superficial burns	—	17.3	48.0	73.4	83.7	1.7
J. S.	71	46.8	224551	Carcinoma of lung	17.0	28.5	34.6	54.0	61.8	0.5
O. H.	15	52.5	236282	Acute rheumatic fever	34.1	49.0	60.2	66.3	73.3	4.7
L. T.	15	57.5	244698	Acute glomerulonephritis	33.1	45.1	52.9	72.3	85.3	0.5
L. J.	49	57.7	614093	Myocardial infarction	12.3	28.0	53.4	—	—	—
H. S.	30	50.2	605941	Rheumatic heart disease	21.2	49.7	71.7	—	—	—

diagnosis in each case is recorded in Table 1; none of these patients presented any clinical evidence of either pancreatic or other disorder involving the digestive system. The 5 patients with pancreatic insufficiency (Table 2) were well known to the gastrointestinal clinic of the University Hospitals. One had had chronic pancreatitis for at least three years, and the remaining 4 had undergone pancreatic ranged from 61.8 to 90.1 per cent of ingested I^{131}, and fecal excretions from 0.5 to 4.8 per cent. In the group with pancreatic insufficiency the urinary excretion for seventy-two hours ranged from 20.5 to 55.8 per cent of ingested I^{131}, and fecal excretions from 24.4 to 63.8 per cent. When pancreatic extract was administered to the same group, the urinary excretion over an equivalent period amounted

Table 2. *Fecal and Urinary Excretion of Isotope after a Test Meal of I^{131}-Labeled Casein in Patients with Pancreatic Insufficiency.*

Patient	Age	Weight	Hospital No.	Diagnosis	Pancreatic Extract Administration	I^{131} Excretion (Percentage Ingested)					
						Urine					Feces
	yr.	*kg.*				*6 hr.*	*12 hr.*	*24 hr.*	*48 hr.*	*72 hr.*	*72 hr.*
J. S.	52	48.5	611320	Whipple operation for carcinoma of pancreas	No	6.9	17.8	37.2	53.6	55.7	26.7
					Yes	10.7	22.9	41.3	57.8	60.3	6.5
S. A.	47	45.0	248241	Whipple operation for ampullary carcinoma	No	3.8	7.8	23.6	39.1	39.7	26.8
					Yes	—	5.9	24.5	48.3	58.0	22.4
M. C.	61	41.2	243067	Chronic pancreatitis	No	4.4	4.7	17.0	35.6	40.0	35.2
					Yes	7.3	21.5	48.3	71.0	76.2	14.1
M. S.	54	68.6	300606	Whipple operation for carcinoma of duodenum	No	3.3	7.8	13.2	19.2	20.5	63.8
					Yes	—	17.7	35.6	51.9	54.1	36.2
B. T.	66	57.5	603487	Whipple operation for ampullary carcinoma	No	11.4	—	36.5	51.9	55.8	24.4
					Yes	9.5	—	35.4	48.9	52.6	35.0

resection for carcinoma two months, one year, two years and four years, respectively, before the present study. All patients with pancreatic insufficiency had required a daily ration of pancreatic extract to control diarrhea and maintain weight.

The subjects without disease of the digestive tract were studied for a single seventy-two-hour period, whereas patients with pancreatic insufficiency were studied during two periods of seventy-two hours each. In the latter group no pancreatic extract was given for six to eight days before or during the first study period. Beginning at least two days before to 52.6 to 76.2 per cent of ingested I^{131}, and the fecal excretion fell to 6.5 to 36.2 per cent. In 2 of the 5 cases the administration of pancreatic extract failed to cause a significant increase in urinary or a decrease in fecal excretion. Total urinary and fecal recovery of I^{131} during the seventy-two-hour collection period varied from 62.3 to 91.0 per cent of that ingested in both the control and pancreatic-deficient groups (with or without pancreatic extract). As a rule, a major portion of the isotope excreted in the feces was obtained during the first twenty-four hours after the test meal.

The blood samples drawn from 3 persons without gastrointestinal disease showed a gradual rise in I^{131} concentration, but in each case the blood samples assayed at only slightly higher than the background level.

Discussion

The fecal excretion of isotope after the ingestion of labeled protein was strikingly different in patients with pancreatic insufficiency and those without gastrointestinal disease. In none of the latter group did this exceed 4.8 per cent of the ingested I^{131}, whereas more than five times this amount was excreted in the feces by each of the patients with pancreatic insufficiency when they were not receiving pancreatic extract. Similar results were obtained by Lavik et al.[2] in children with cystic fibrosis of the pancreas. It is therefore evident that the determination of the fecal excretion of isotope after a test meal of I^{131}-labeled protein can be a useful technic in the evaluation of protein digestion and absorption in patients believed to be deficient in pancreatic function.

Urinary values are influenced not only by the digestive and absorptive process but also by factors controlling the storage and degradation of the absorbed amino acids. This is evident from the variability in the combined fecal and urinary excretion of isotope (62.3 to 91.0 per cent) in all patients given the test meal, as well as in the amount of isotope excreted in the urine of the control patients (61.8 to 90.1 per cent). In the presence of these modifying influences, it is not surprising that the urinary values did not differentiate the two types of patients as clearly as the fecal values. Nevertheless, most of the patients with pancreatic insufficiency excreted much less of the ingested isotope in the urine than the controls (Fig. 2), and only occasionally did the urinary values in the two groups overlap. It is possible that an even more striking difference would have been observed if truly normal

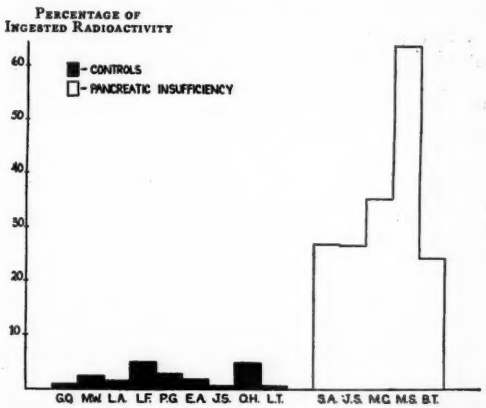

Figure 1. *Fecal Excretion of Isotope during a Seventy-Two-Hour Period after a Test Meal of I^{131}-Labeled Protein.*

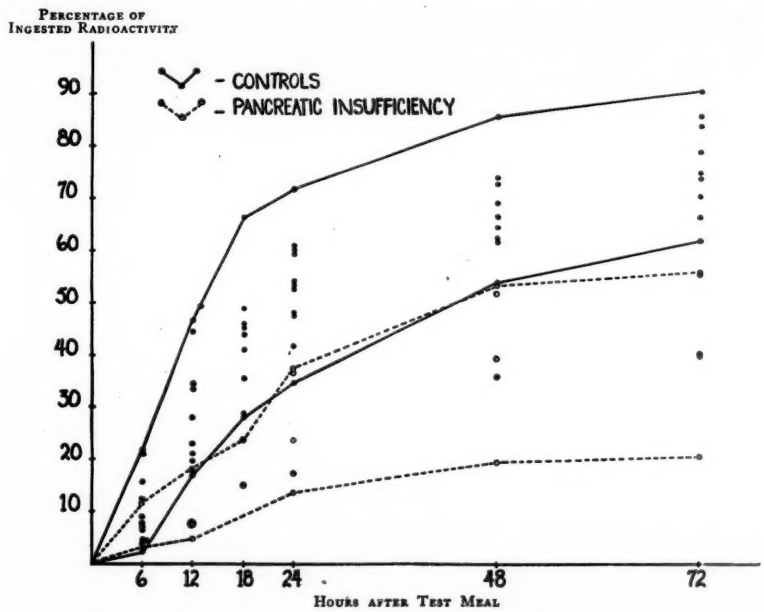

Figure 2. *Urinary Excretion of Isotope after a Test Meal of I^{131}-Labeled Protein.*

subjects had been employed as controls. Except in borderline cases, therefore, the urinary excretion measurements after a test meal of labeled protein might be of some value as a diagnostic aid and as a crude index of protein digestion and absorption.

When pancreatic extract was administered, 3 out of the 5 patients with pancreatic insufficiency showed a definite decrease in the fecal excretion of I^{131} after the ingestion of labeled protein. This response to pancreatic extract lends support to the use of I^{131}-labeled protein for evaluation of protein digestion and absorption in such patients. Failure to obtain a more normal absorption of protein when pancreatic extract was administered does not necessarily mean that these patients were unable to absorb the products of protein digestion, for it could also have been due to an inadequate hydrolysis of the relatively large quantity of protein included in the test meal. Thus, in a similar study in children with cystic fibrosis of the pancreas, 1 child who absorbed no more than 60 per cent of the administered protein, given with or without pancreatic extract, readily absorbed pre-hydrolyzed protein.[2]

Summary and Conclusions

The fecal and urinary excretion of I^{131} was measured for seventy-two hours after the administration of a test meal containing I^{131}-labeled protein to patients with and without pancreatic insufficiency.

Fecal excretion in the patients with pancreatic insufficiency was significantly greater than that in patients with no disease of the gastrointestinal tract.

Although the urinary excretion of isotope averaged significantly less in the patients with pancreatic insufficiency, the difference in urinary excretion between the two groups was not as striking as that in fecal excretion.

The administration of pancreatic extract with the test meal decreased the fecal excretion and increased the urinary excretion of I^{131} in 3 out of 5 patients with pancreatic insufficiency.

References

1. Lavik, P. S., and Miller, R. W. Use of I^{131}-labeled protein in study of protein digestion and absorption. Western Reserve University Atomic Energy Research Project, Report No. NYO-1623, April 16, 1951.
2. Lavik, P. S., Matthews, R. W., Buckaloo, G. W., Spector, S., and Friedell, H. L. Use of I^{131}-labeled protein in study of protein digestion and absorption in children with and without cystic fibrosis of pancreas. *Pediatrics* (in press).
3. Fine, J., and Seligman, A. M. Traumatic shock. VII. Study of problem of "lost plasma" in hemorrhagic tourniquet and burn shock by use of radioactive iodoplasma protein. *J. Clin. Investigation* **23**:720-730, 1944.
4. Warren, S., and Dixon, F. J. Antigen tracer studies and histologic observations in anaphylactic shock in guinea pig. Part I. *Am. J. M. Sc.* **216**:136-145, 1948.
5. MacIntyre, W. J. Scintillation counter for measurement of I^{131} uptake in thyroid gland. *Proc. Soc. Exper. Biol. & Med.* **75**:561-565, 1950.

EXPERIENCE WITH A TUBELESS METHOD OF GASTRIC ANALYSIS*

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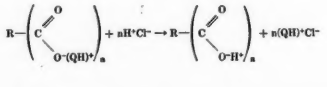
BOSTON

THE recent availability of cation-exchange indicator compounds has suggested their use in determining the presence or absence of free hydrochloric acid in gastric contents without the need for intubation of the stomach.[1, 2] The purpose of this preliminary report is to present our experiences with this test in comparison with the conventional tube method of gastric analysis, and to outline the indications and limitations of the tubeless technic.

Rationale

The cation-exchange indicator compound Diagnex§ is prepared by replacing the hydrogen cation of a carboxylic acid group, present in the exchange resin, with a quininium cation. As demonstrated by in vitro and in vivo studies,[1] the free hydrogen cations of dilute hydrochloric acid solutions and human gastric juice readily displace the quininium ion according to the following formula:



The released quinine is absorbed in the small intestine, and approximately a third is excreted in the urine.[3]

The urinary excretion begins within fifteen minutes of absorption and continues at fairly high levels for three or four hours. The first two hours after the oral administration of the indicator compound comprise the critical period in the determining of the presence of free hydrochloric acid in the stomach by urinary quinine excretion. Quinine found in later urine specimens may not be related to the presence or degree of free acidity in the stomach.

Method

The quininium resin indicator compound was administered orally in a 2-gm. dose of granules

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§Kindly supplied by E. R. Squibb and Company, New York City.

(containing 36 mg. of available quinine) to the patient after an overnight fast and after stimulation of the parietal cells of the stomach with histamine, 7 per cent alcohol or caffeine sodium benzoate. A control sample of urine and specimens voided one and two hours after the administration of the resin were collected and examined for quinine content by measure of their fluorescent intensity against standard solutions under ultraviolet light.[4] The amount of quinine present was graded from 0 to ++++. The determination of free acidity in the samples of gastric juice obtained by the conventional method of fractional gastric analysis was performed by titration with Töpfer's reagent and phenolphthalein in the usual manner. Because of urgent clinical considerations and active symptoms, several of the subjects used in this study did not fast the full ten hours, and a number did not receive any parietal-cell stimulant. In no case was the validity of the quinine-excretion test compromised by this deviation from the standard technic.

Directions for the Test

The patient has nothing to eat after midnight and takes no breakfast.

The morning urine obtained on rising is discarded.

A secretory stimulant — either 0.5 mg. of histamine diphosphate base subcutaneously when no contraindications exist, caffeine sodium benzoate, 250 mg. orally in water, coffee or tea (without sugar or cream) or 50 cc. of 7 per cent alcohol orally — is administered.

A control urine specimen is obtained twenty minutes after the histamine has been given (one hour after caffeine or alcohol).

Diagnex granules are administered in a glass of water. Granules do not dissolve and should not be chewed.

All the urine voided one hour and two hours after administration of the Diagnex is collected and saved in separate containers.

Determining Quinine in Urine

The three urine specimens (control, one-hour sample and two-hour sample) are analyzed separately.

The urine specimen is diluted to 300 cc. and mixed; 30 cc. of diluted urine is poured into a graduated separatory funnel and 0.5 cc. of a normal solution of sodium hydroxide and 15 cc. of ether are added.

The container is corked with a glass stopper and shaken five times lightly, and the ether and urine are allowed to separate. If an emulsion forms, several drops of 95 per cent alcohol are added.

The urine and ether are drawn off to the 8.2 cc. mark (leaving 8.2 cc. of ether), and 5 cc. of one-tenth normal solution of sulfuric acid is added. The mixture is shaken five times lightly and allowed to separate. Quinine is in the bottom layer of sulfuric acid.

The solution of sulfuric acid is drawn off and compared with known standards or recorded as 0 to ++++ under ultraviolet light.

Free hydrochloric acid is present in the gastric contents if more than 25 microgms. of quinine is found in the urine sample. Readings of less than 15 microgm. are reported as negative, and those of 15 to 25 microgm. as a trace. The test may be repeated after five days.

Material

The technic described above was utilized in 58 examinations on 54 subjects, equally divided between men and women, the ages ranging from twenty-three to eighty-seven years. Control gastric analysis by the usual intubation technic was performed in 50 of these subjects. Histamine was used as the parietal-cell stimulant in 24 cases, and caffeine and alcohol in 1 case each. Contraindications such as angina pectoris, active gastrointestinal bleeding, severe ulcer pain and allergy precluded their use in the remainder.

The subjects examined included the following classifications. Five normal healthy men under thirty-five years of age were tested as controls. There were 15 patients under medical treatment for duodenal ulcer, 7 of whom were examined during episodes of active bleeding. Ten additional patients were studied at various intervals after major operations for duodenal ulcer (9 cases of subtotal gastrectomy and 1 case of vagotomy with posterior gastroenterostomy). In this surgical group 3 patients were tested both preoperatively and postoperatively. The remaining patients included 4 cases with gastric ulcer, 4 with gastric carcinoma, 1 with gastric polyps, 2 with gastritis, 2 with hiatus hernia, 2 with biliary-tract disease, and 1 each with dyspepsia of unknown cause, diverticulitis and pulmonary carcinoma. All the gastrointestinal lesions were confirmed by roentgenographic diagnoses, and some in addition by operation or gastroscopy. Six patients with anemia were studied: 2 with pernicious anemia, 2 with a nonpernicious macrocytic anemia, and 2 with an iron-deficiency anemia.

Results

Free acid (+ to +++) was demonstrated in all 5 healthy controls by the tubeless-analysis technic. When studied by the standard intubation technic 3 of these controls were found to have from 6 to 16 units of free acid, and 2 controls who experienced marked retching with the tube were found to have no free acid in the gastric contents.

The results of examinations on 25 patients with duodenal ulcer were divided into those treated medically and those treated surgically. Of 15 medical patients, 13 had + to +++ tests for free acid by the tubeless method and 5 to 30 units by the tube technic. Two patients with duodenal ulcer had no

free acid by the tubeless analysis; 1 of these had 10 units of free acid by aspiration, and the other refused the tube. Of 10 patients with ulcer studied postoperatively, 8 had no free acid, both by tubeless and tube technic. The remaining 2 had a + test for free acid by the exchange-resin method and 5 and 20 units by aspiration. Three of the surgical patients studied preoperatively showed free acid by both methods, and of these, 2 showed no free acid after operation by either method.

The 4 patients with gastric ulcer had + to ++++ tests for free acid by the tubeless analysis and 10 to 76 units by the conventional tube technic. Four patients with gastric cancer, 1 with gastric polyps, and 2 with gastritis had no free acid by either test. All these patients were given histamine as a secretory stimulant.

Two patients with pernicious anemia and 1 with a nonpernicious macrocytic anemia had no free acid after histamine stimulation by either method. Another patient with nonpernicious macrocytic anemia had no free acid by the exchange-resin test whereas there were 10 units of free acid by the aspiration technic. Two patients with an iron-deficiency anemia refused to take a gastric tube but had ++ tests for free acid by the tubeless method.

In the entire series there were 12 patients who were studied during an episode of acute gastrointestinal bleeding, including 9 with duodenal ulcers (before or after operation), 1 with gastric ulcer, and 1 with hiatus hernia. Ten of these patients had readings of + to +++ and 6 to 30 units of free acid. One patient with bleeding duodenal ulcer and 1 with bleeding gastric cancer had no free acid by either test.

There was failure of correlation between the two tests in only 4 cases. One patient with duodenal ulcer showed only a trace by the exchange technic and 10 units of free acid by aspiration; 1 with nonpernicious macrocytic anemia had no free acid by exchange resin and 10 units by aspiration. Two of the normal controls with ample free acid by the exchange technic failed to demonstrate free acid by a conventional intubation test that was characterized by considerable retching.

No untoward reactions were observed in any of the patients who were given the indicator resin. There were no gastrointestinal disturbances after the ingestion of the resin, with the exception of 1 patient who vomited the material on the seventh postoperative day after a subtotal gastrectomy. On the basis of studies of blood and urine performed before and after the use of the exchange resin, no deleterious effects were discernible.

Discussion

This study confirms the findings of Segal[1] that the tubeless method of gastric analysis is a valid test of the presence of free hydrochloric acid in the stomach. In the 58 examinations reported here-with free acid was demonstrable in the clinical conditions in which it could be expected, such as active duodenal and benign gastric ulcers, and not demonstrable in known achlorhydric entities such as pernicious anemia, gastric cancer and atrophic gastritis. Only 2 examinations by the tubeless method failed to show free acid when it was detected by the conventional technic. It should be clearly understood that the indicator resin tests the ability of the stomach to secrete free hydrochloric acid and does not measure pH or units of acid. Although it is a grossly quantitative test, its interpretation as such is unreliable and is not recommended.

Certain clinical conditions seem to present special advantages for the use of the tubeless method. The interpretation of the standard fractional gastric analysis performed in patients who have had a subtotal gastrectomy has always been suspect because of uncertainty about the position of the tube in the gastric remnant and because of the variable factor of regurgitation of neutralizing juices from the duodenum and jejunum back through the stoma. It was expected that the indicator resin would obviate these disadvantages. In the 9 patients who were studied after gastric resection there was excellent correlation between the indicator-exchange method and the standard aspiration technic. Under certain conditions it is possible that the resin leaves the gastric remnant before the hydrogen ion can enter into chemical reaction and thus yields a falsely negative result.

The use of antacid therapy during active bleeding from a duodenal ulcer has been a controversial subject and is not generally regarded as essential.[5] It has been suggested that there may be a temporary hypoacidity or anacidity in the stomach during active gastrointestinal bleeding. Ample amounts of free hydrochloric acid were demonstrated in 9 of 10 patients with a bleeding peptic ulcer despite the fact that no gastric secretory stimulant was administered to any patient in this group. This preliminary observation suggests that antacid therapy should be incorporated into the medical management of bleeding peptic ulcers. Under such conditions the exchange-resin technic affords a simple method for evaluating the need for more intensive antacid therapy.

The passing of a stomach tube presents special problems and contraindications in certain patients.[6] During active bleeding from the upper gastrointestinal tract, whether from an unidentified source or from a known intrinsic lesion of the lower esophagus or stomach, the insertion of a stomach tube to test for free acid is considered hazardous and inadvisable. Patients with angina pectoris or recent myocardial infarction are likewise unfavorable subjects for the conventional technic of gastric analysis. Persons with great emotional instability or hyperactive gag reflex may present considerable difficulty in the passing of a tube and contribute

unintentionally to an erroneous report of achlorhydria. Thus, it has been shown that nausea and retching produced by the tube may inhibit histamine-stimulated gastric secretions[7] and may cause regurgitation of alkaline duodenal juices, which can neutralize gastric acid. The neutralizing capacity of excessive saliva on gastric acidity has also been demonstrated.[8] Of the 5 normal adults used as controls in this study, 2 who experienced severe retching and regurgitation with the gastric tube had no free acid on conventional analysis but showed +++ tests for free acid by the indicator-exchange technic. In all the conditions outlined above, the exchange resin makes it possible to determine the presence of free hydrochloric acid in the stomach without danger or discomfort to the patient.

The tubeless gastric analysis has been advocated by Segal and his co-workers[9] as a screening test for achlorhydria with emphasis on the early detection of gastric cancer. The test can be performed by the patient without the need for trained medical personnel, and the urine specimens may be examined later in the day. The method of laboratory analysis, however, does not lend itself to routine office use without technical assistance.

Contraindications to the test at present seem limited to subjects with known quinine sensitivity, persistent vomiting and perhaps advanced renal disease. The procedure will need further evaluation to determine its reliability in the presence of diarrhea. The small amount of quinine used (36 mg.) does not present any problem of toxicity from the size of the dose. The data obtained under the clinical conditions reported in this study suggest that the routine use of a gastric secretory stimulant, such as histamine, alcohol or caffeine, is not essential to obtain reliable results and that such agents need not be employed on the first testing.

The tubeless gastric analysis will probably not replace the conventional tube technic as a routine procedure that has proved itself to be simple, less expensive and less protracted. In specific clinical situations, however, the indicator-exchange technic has distinct advantages that warrant its wider use.

Summary

A cation-exchange indicator resin has been utilized to determine the presence or absence of free hydrochloric acid in gastric contents without intubation.

Experience with 58 examinations on 54 subjects is reported.

The test can be utilized easily under clinical conditions and affords an excellent correlation with results obtained by the standard tube technic of fractional gastric analysis.

The tubeless analysis can be used advantageously in the presence of active bleeding from the upper gastrointestinal tact, angina pectoris, recent myocardial infarction, emotional instability and hyperactive gag reflex and after subtotal gastric resection.

Contraindications include quinine sensitivity, persistent vomiting and advanced renal disease.

References

1. Segal, H. L., Miller, L. L., Morton, J. J., and Young, H. Y. Use of cation exchange indicator compounds to determine gastric acidity without intubation. *Gastroenterology* **16**:380-386, 1950.
2. Segal, H. L. Determination of gastric acidity without intubation. *M. Clin. North America* **33**:593-602, 1951.
3. Goodman, L., and Gilman, A. *Pharmacologic Basis of Therapeutics.* 1383 pp. New York: Macmillan, 1941. P. 910.
4. Kelsey, F. E., and Geiling, E. M. K. Micro determination of quinine in blood and tissues. *J. Pharmacol. & Exper. Therap.* **75**:183-186 1942.
5. Bockus, H. L. *Gastroenterology.* Vol. 1. 831 pp. Philadelphia: Saunders, 1944. P. 601.
6. *Ibid.* P. 609.
7. Grossman, M. I., Wooley, J. R., Dutton, D. F., and Ivy, A. C. Effect of nausea on gastric secretion and study of mechanism concerned. *Gastroenterology* **4**:347-351, 1945.
8. Zaus, E. A., and Fosdick, L. S. Effects of saliva upon gastric digestion. *J. Dent. Research* **14**:3-13, 1934.
9. Segal, H. L., Miller, L. L., and Morton, J. J. Detection of achlorhydria by tubeless gastric analyses. *J. Nat. Cancer Inst.* (in press).

CARCINOMA DIAGNOSED BY EXAMINATION OF PERICARDIAL FLUID*

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THE incidence of metastatic tumors of the heart and pericardium has been reported as 6 to 10 per cent of all malignant neoplasms.[1] There are few reports of the ante-mortem diagnosis of this condition. Pericardial effusion is often but not regularly present. McCandless and Faloon[1] state that there are only 10 cases in the American literature of metastatic disease of the heart and pericardium in which accurate diagnosis was made during the life of the patient. Heninger,[2] in 1934, cited only 5 cases of metastatic tumor of the heart and pericardium in which the diagnosis was made before death. The same author reports a case of his own in which the diagnosis was made during the life of the patient. On x-ray study of the chest a carcinoma of the right upper lobe was seen before pericardial fluid appeared. A pericardial aspiration revealed malignant cells.

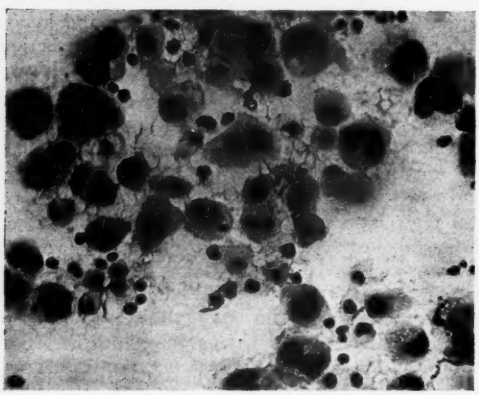

FIGURE 1. *Malignant Cells in the Pericardial Fluid in Case 1.*

Scott and Garvin,[3] in an excellent report of 118 cases of metastatic tumor of the heart and pericardium, found involvement of the pericardium in 70 per cent at autopsy. However, in only 22 per cent was there acute pericardial disease that could have been detected during life. These authors also point out that 35.6 per cent of metastases to the heart and pericardium have their primary site in the bronchus. Shanks and Kerley[4] state that carcinoma of the lung, especially of the apex of the left lower lobe, frequently invades the pericardium and may result in the rapid development of a large pericardial effusion. Invasion of the pericardium is most commonly due to direct extension. Hematogenous dissemination and lymphatic spread are less common. Zemansky,[5] in a study of body fluids for tumor cells, correlated 113 cases with subsequent tissue examination and reported a case of carcinoma of the pericardium in which the diagnosis was made ante mortem. Honigman,[6] investigating tumor cells in serous effusions, reported 90 cases of carcinoma of all types, and in 1 case pericardial effusion was due to metastatic disease secondary to carcinoma of the breast.

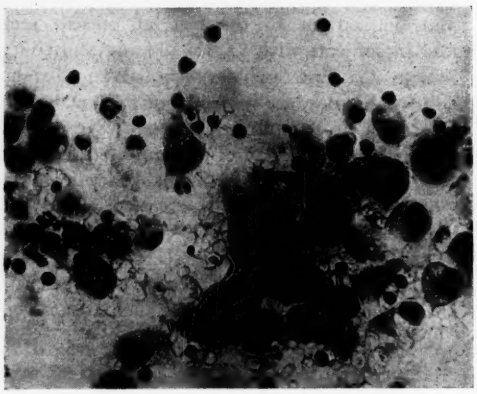

FIGURE 2. *Malignant Cells in the Pericardial Fluid in Case 2.*

It is evident, therefore, that ante-mortem diagnosis of malignant pericardial effusion has not been frequently made. In view of the recent emphasis on cytologic methods of examining body fluids in cancer diagnosis, the following cases are reported.

CASE REPORTS

CASE 1. S. F., a 62-year-old man, entered the hospital on March 22, 1951, with the chief complaints of shortness of breath and weight loss of several months' duration.

Physical examination revealed palpable right supraclavicular lymph nodes. The lungs showed dullness to flatness at both bases posteriorly with diminished breath sounds.

X-ray study demonstrated an enlarged, aortic type of heart, with a pericardial effusion that had not been present on

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previous examinations. An atelectasis of the right middle lobe was present, with a concomitant pleural effusion. A pericardial aspiration was performed, and 250 cc. of hemorrhagic fluid was removed and air injected into the pericardial sac. Pathological examination showed many atypical cells, suggestive of cancer (Fig. 1). A biopsy taken from the supraclavicular lymph nodes was reported as showing anaplastic carcinoma, possibly from stratified squamous epithelium. Two serial x-ray studies demonstrated atelectasis of the right middle lobe, with pleural effusion at both bases. On April 5, after a thoracentesis, the patient suddenly became apneic; he died 14 days after admission.

CASE 2. M. S., a 52-year-old woman, was admitted to the hospital for the first time on May 29, 1948, with complaints of dyspnea and orthopnea of 2 weeks' duration.

Physical examination revealed an acutely ill woman with a temperature of 102°F. Supraclavicular nodes were felt bilaterally. The liver edge was palpable 4 fingerbreadths, below the costal margin.

X-ray study of the chest disclosed a bilateral pleural effusion. A thoracentesis was performed, and 125 cc. of straw-colored fluid was removed from the left side. A negative pathological report for cancer was returned. A pericardial effusion was noted on the second x-ray film, and 200 cc. of hemorrhagic fluid was removed from the pericardial cavity followed by air injection. Pathological examination showed malignant cells (Fig. 2). A search for the primary site was fruitless. Biopsy of several supraclavicular lymph nodes demonstrated metastatic carcinoma. A bronchoscopy performed during a subsequent hospital admission revealed primary bronchogenic carcinoma of the right lung. The hospital course was gradually downhill, and the patient died on January 4, 1949.

DISCUSSION

As illustrated in the cases presented above, the microscopical study of body fluids is important in accurate ante-mortem diagnosis. This is especially borne out in the older age groups.[7] In Case 1 the pericardial effusion was a later manifestation but a confirmatory sign of malignant neoplasm. In Case 2 pericardial effusion was the initial sign of bronchogenic carcinoma. Although Shanks and Kerley[4] emphasize left-sided bronchogenic carcinoma as responsible for pericardial metastases, both these patients exhibited carcinoma in the right lung that was responsible for the pericardial involvement. Suspicion of cancer should be aroused particularly in the presence of hemorrhagic pericardial effusion in elderly patients. A careful cytologic examination of body fluids is important. In such cases one should think of the bronchial tree as a primary site of the lesion.

SUMMARY

Two cases of hemorrhagic pericardial effusion are presented.

In 1 case pericardial effusion was the primary sign of a malignant lesion.

Metastatic pericardial effusion secondary to carcinoma of the lung was proved before death in both cases.

REFERENCES

1. McCandless, F. D., and Faloon, W. F. Diagnosis of metastatic tumor by cytological examinations of pericardial fluid: report of case using Shorr's stain. *Ann. Int. Med.* **29**:1157-1168, 1948.
2. Heninger, B. R. Clinical aspects of pericardial metastasis. *Ann. Int. Med.* **7**:1359-1369, 1934.
3. Scott, R. W., and Garvin, C. F. Tumors of heart and pericardium. *Am. Heart J.* **17**:431-436, 1939.
4. Shanks, S. C., and Kerley, P. *Textbook of X-Ray Diagnosis.* Second edition. Vol 2. 702 pp. London: H. K. Lewis Company, Ltd., 1951. P. 162.
5. Zemansky, A. P. Examination of fluids for tumor cells: analysis of 113 cases checked against subsequent examination of tissue. *Am. J. M. Sc.* **175**:489-504, 1928.
6. Honigman, A. H. Significance of tumor cells in serous effusions. *Surg., Gynec. & Obst.* **81**:295-301, 1945.
7. Sahn, S. H., Leichtling, M., and Bass, H. E. Significance of pleural effusion in patients past age of fifty, *New Eng. J. Med.* **246**:927, 1952.

MEDICAL PROGRESS

CONTRIBUTIONS OF THE SOCIAL SCIENCES TO THE SOLUTION OF HEALTH PROBLEMS

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RELATIONS between medicine and the social sciences, long a field for interesting discussion, have been explored intensively from both sides of the fence in recent years. It is convenient arbitrarily to separate the natural sciences, such as chemistry, physics and biology, from the social sciences, including sociology, social anthropology and social and personality psychology. Psychology, usually grouped under the social sciences, is sometimes considered a natural science. Strictly speaking, mathematics falls into neither group but is used by both. Probably many physicians practicing today have had relatively little contact with the social sciences in their premedical education. It is comparatively difficult, therefore, to understand precisely how activity in the social sciences relates to medicine. This article attempts to specify this relation in a rudimentary way, making no pretense of covering the field completely.

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NEW FORCES IN SOCIETY

World society is deeply stirred by emergent forces threatening to overrun the flimsy levees created by previous generations. These new forces make it imperative for physicians to view their field broadly if they are to provide the comprehensive type of health service made possible by modern knowledge and modern facilities.

Among the more important of these forces are increasing industrialization and urbanization, resulting in a shift from relative independence to greater interdependence. Mass production also makes more leisure possible. With the end of the

frontier came recognition of the need for conservation of resources and of planning for their most effective use. Increased life expectation at birth, resulting both from greater application of preventive medicine and from improved economic standards, creates the problem of what to do with the increasing proportion of aged persons in the population and with the chronic diseases to which they are prone. Limitation of family size and greater geographic mobility of the population have altered housing arrangements, which increases the problem for older family members who no longer find a useful place for themselves in a small household for which needed consumer goods are mass produced.

The old laissez-faire economy is more or less yielding to a controlled economy, although the shift may be less marked in the United States with its abundant resources than elsewhere in the world. A leveling of incomes after taxes is quite evident (with lower incomes increasing in proportion and higher ones diminishing),[1] and this has reduced medical philanthropy. The important interrelation of food supply and population causes greater and greater concern in many parts of the world.

The concept of the dignity and worth of the individual increasingly pervades the thought of the free world. Racial discriminations are breaking down, and demands for equal civil rights become more and more effective in most countries. The idea of social security as a right and a necessity in a world where willingness to work can no longer ensure a livelihood has quite generally replaced the old idea of charity for those who through indolence or disease aroused the sympathy of their fellows.

Although many newly established countries and former colonies of the world are strongly nationalistic, the need for world co-operation is realized. The idea of the brotherhood of man in a community of nations with world-wide perspective finds expression in the health field in such organizations as the World Health Organization and the World Medical Association. With technical assistance to underdeveloped areas of the world comes the necessity for understanding diverse cultures if proffered help is to be accepted and to achieve its desired end.

Because of wider and broader education people have learned the value of modern medicine in relieving and preventing sickness. New health attitudes are resulting from intelligent health education. Alcoholism, for example, is coming to be regarded as a disease, not simply a crime, and venereal disease as an illness, rather than a just punishment for sexual aberration. Mental health is thought of as a desirable and possibly attainable end. The idea is widespread that financial support of research will eventually solve many remaining disease problems, and greater support comes from both voluntary health agencies and government.

All these attitudes produce new problems for the medical profession itself, and for patients and potential patients living under conditions of such rapid change. The foundations of life are shaken, and many of the "social technics," as Ruesch[2] calls them, learned in early life are no longer effective. These conditions of change, like the adverse social conditions and social maladjustments studied by Robinson,[3] "are disturbing to health because they produce excessive emotional reaction and emotional strain." Plant,[4] accepting "the hypothesis that personality and environment are mutually impinging sets of forces," would doubtless agree that present-day forces produce an environment causing such rapid personality readjustment as to constitute a serious danger for many people.

Bluestone[5] says, "We need a stereoscopic view of the patient which will combine the social and the medical aspects of illness in a picture which has added life and depth." And Cherkasky,[6] who worked with him at the Montefiore Hospital, follows the same line of thought:

> To understand what caused this patient to become sick, it is necessary to know what sort of family he has, where he lives, what kind of clothes he wears, what food he eats, what kind of employment he has, and how he reacts to these factors. These and similar facts make up man as a social being, and may be more provocative in the origin of his disease than the germ which has been isolated from his sputum in the bacteriological laboratory. The hospital must seek a knowledge of these factors as eagerly as it seeks knowledge in the field of scientific medicine.

How *can* medicine be truly scientific if the social elements in disease causation are slighted? Sydenstricker[7] has admirably described man's environment, and the following quotation is pertinent to this discussion:

> In the first place there is a physical environment in which innumerable conditions and relations may affect, directly or indirectly, health. The more advanced the civilization, the greater is the alteration of physical environment that man has accomplished.
>
> In the second place, the population itself constitutes a part of the total environment. We speak of this as *social* environment, and the more we study it, the more we are impressed with its importance as a factor in determining the physical and mental well-being of the population and the rate at which individual members survive. In every group of human beings there exist certain social relations and modes of social behavior. The community has not only a geographic habitat but also a social structure. The individuals composing the community are clustered in families, associated into overlapping groups for trade, occupation, religion and amusement; separated into classes differentiated by caste and economic achievement; swayed as a mob from one course of social action to another; guided by newly acquired knowledge, such as inventions or discoveries of ways in which to escape or cure disease. Tradition, superstition, and mores; modes of living, fads and fashions; standardization of ideas and attitudes by the press, movies, radio and schools; cultural factors, such as the esthetic idea of posture or a religious regimen of diet or of personal cleanliness — these go to make up our social environment and constitute conditions that may influence health in an even greater degree than physical surroundings. Again, in considering social

environment, not only the social surroundings that exist at any given instant in time but the process of change must be taken into account as possible factors.

Physicians may profitably look on the social-science side of the fence, referred to in the opening paragraph, to discover which of the problems the social scientists are investigating have a bearing on the health questions that doctors, on their side of the fence, are seeking to solve.

Social-Science Research on Health

The focus here is on man as a unit in society and on the groups human beings form in carrying on their activities. The social sciences may well be called the sciences of human relations or human behavior. In practice the field has been subdivided into a number of more or less overlapping disciplines, with certain fringe areas. Some of the major subdivisions are dealt with individually below, and areas of recent investigation related directly or indirectly to health are mentioned. To aid in clarification, definitions of each of the major fields are given. Caudill,[8] the Health Information Foundation,[9] Lippitt[10] and Hall[11] are among those who have recently summarized social-science research pertinent to the health field.

Demography

Demography, "the science of population, is concerned with composition and movement of populations and with the laws that control population growth, decline and migration."[12] Censuses are much more complete than formerly, with a great deal of valuable intercensal material obtained by sampling technics. Registration of births and deaths is reasonably complete, but only in the United Kingdom is there much material on the relation of mortality rates to social classes. Since 1831, when William Farr joined the British General Register Office, British vital statistics have been outstanding, contributing many valuable data on differential mortality.[13, 14] Morbidity data are even less readily available; Collins[15] has presented an admirable discussion of this problem. Turner[16] has collected a useful bibliography of studies made over a period of years on the population of Hagerstown, Maryland, and a number of useful studies have been made in the Eastern Health District, adjacent to the Johns Hopkins University School of Hygiene in Baltimore.[17]

In larger cities the census is made by relatively small units of more or less homogeneous population known as census tracts. When mortality and morbidity data are recorded according to these tracts, accurate rates may be computed and areas located in which special problems exist.

Population problems are being intensively debated in many parts of the world. A few countries have been troubled because of declining population,[18, 19] but even greater problems loom because of excessive increases in certain areas. As Hackett[20] says:

> Public health has proved to be the most successful of the applied social sciences — so much that in backward countries, economic and educational measures have been unable to keep pace. That is why we have a population problem in underdeveloped areas, but it is hard to see why the entire blame should rest on the agencies of public health.

To explain the four-fold increase in world population in the past three hundred years, and the doubling of life expectancy at birth in North America and Western Europe that is a more recent development, Dorn[21] cites four factors:

> . . . primarily responsible for man's increasing control over his environment:
>
> (a) the opening up of new continents, which provided additional sources of food, precious metals and other commodities as well as an outlet for the surplus population;
>
> (b) the expansion of commerce, which made possible the transportation of food and capital goods over long distances;
>
> (c) technological changes in agriculture, together with the development of modern industrial processes; and
>
> (d) increased control of disease through improved housing, better food and water supplies, adoption of sanitary measures, the growth of the knowledge of preventive medicine, and more recently, discoveries in pharmacology and chemotherapy, particularly the antibiotics and newer insecticides.

Sax[22] discusses the population problem, giving a number of interesting references.

Statistics

Sand[23] says, "Exact knowledge can only be based on measurement of objects," pointing up the importance of statistics to progress in the social sciences. In fact, "the statistical method is so essential to the social sciences and has been so greatly developed in their use that statistics is commonly grouped with the social disciplines."[12] This is not the place to discuss the remarkable development of the statistical method. It serves to offset somewhat the difficulties experienced by social scientists because controlled experimentation is so rarely available to them. With proper statistical handling, it is often possible to make allowances for a number of variables not otherwise controllable. The theory of probability, correlation and partial correlation, as well as sampling technics, are especially important statistical tools. Obviously, the widespread use of machine punch-card methods permits computation with greater speed and accuracy then would be possible otherwise.

Sociology

Sociology, ". . . the science of society . . . studies situations in which human beings are in relationship with one another. It analyzes the forms of group organization . . . seeks to explain social institutions, standards, cultures, and the forces that operate in social change, such as leadership and invention."[12] To the sociologist the community

is a constellation of social institutions such as the basic cultural institutions of the family, church and school; economic and communications institutions; recreational and health institutions; and institutions of formal social control, such as government. In the sociologic sense, an "institution" is not thought of as a building of brick and mortar like a hospital, but rather as a generally accepted and stylized set of arrangements for dealing with recurrent human relations of everyday life.

The community is also thought of as a constellation of social groupings. Warner and his associates[23a-28] found six clearly defined social classes in studies of a New England community, but his findings are not accepted as universally applicable.[29] Nevertheless, the concept of social groups in American society is of great importance to health workers. The disparity of morbidity and mortality rates among various social classes was mentioned above under "Demography." As another example, Kinsey and his co-workers[30] noted great variation in sexual behavior according to social level and concluded that "Most of the tragedies that develop out of sexual activities are products of this conflict between the attitudes of different social levels" and that ". . . this conflict between sexual patterns is, however, not recognized by the parties immediately concerned, because neither of them understands the diversity of patterns which exist at different social levels."

The word "community" itself is difficult to define because of the diversity and complexity of community life. However, Young[31] says that a local community (which is comparatively easy to understand) always "(1) occupies a territorial area; (2) is characterized by common interests and (3) common patterns of social and economic relations; (4) derives a common bond of solidarity from the conditions of its abode; (5) has a constellation of social institutions and (6) is subject to some degree of group control."

Communities have growth patterns somewhat comparable to those of individuals,[32-35] and it is usually in certain blighted areas that health and social problems are concentrated. Faris and Dunham[36] found that certain types of mental disorder tend to be concentrated in such areas.

Buell and his associates[37] have recently grouped community welfare problems into those related to dependency, maladjustment, ill health and the need for recreation, and have shown that a small group comprising only about 6 per cent of the community's families account for a large proportion of the total problems of the community's health and welfare. If a concentrated and co-ordinated attack on this group is made, more efficient solutions may be anticipated.

Murdock[38] considers the breakdown of the American neighborhood a most serious problem:

> The reasons are obvious, of course. Social and geographical mobility creates a high turnover in neighborhood membership and prevents neighborly ties from crystallizing. Multiplicity of religious sects often makes it impossible for a single church to become a genuine community center. Automobiles and rapid-transit facilities carry residents out of the neighborhood to work, to shop, and to find recreational outlets. Social ties are thus widely dispersed, with the result that neighbors have less and less in common.

The family is probably the social institution most important in the development of personality and hence a source of personality problems as well as personality strength. Richardson,[39] who made intensive family studies of patients in the Cornell Medical Center, says that "the profession of medicine progressed from the diseased organ to the total personality of the patient, and is now ready for the concept of the individual as a member of a family in its community setting."

Following a similar train of thought, Simmons[40] considers the family as the point of convergence of the "micro" and "macro" approaches to life. The former enlarges progressively from microorganism, to organ, organ system, the body as a physical unit and thence to the "whole person" and to his family; the latter begins with the nation or state, narrowing its focus in turn to ethnic or racial subgroups, occupational subgroups, the community and then the family. He suggests that the family is probably the most fruitful unit for cooperation of "micro" and "macro" workers.

In providing the kind of guidance his families need, the physician must understand, among many other things, marriage counselling (there is an association of professional marriage counsellors in this country), problems of separation and divorce, child placement and adoption, and the causes and effects of family disorganization.

The aged group has been studied a great deal. Simmons[41] points out the problem they present in a rapidly changing society: "In the long and steady strides of a social order the aged find themselves fixed and favored in position and performance, but when conditions become unstable and the rate of change reaches a galloping pace the more youthful find opportunities in their favor and may become much earlier seated in the saddle." The latter condition now prevails, of course.

Sociologists are concerned with the division of labor represented by various professions, with the status various groups hold in the community and with the roles individuals play under varying conditions.

Parsons,[42] as a sociologist, views medicine from a point of view that may help medicine's understanding of itself. He classifies the medical profession as being characterized by "*rationality*" in its search for objective truth, noting that "the present degree of valuation of rationality as opposed to traditionalism is rather 'unnatural' in the sense that it is a highly exceptional state in the

world at large." The profession also has "functional specificity" owing to the high degree of technical competence required, but "the technical competence which is one of the principal defining characteristics of the professional status and role is always limited to a particular 'field' of knowledge." It is, in addition, "universalistic" in having "standards and criteria independent of the particular social relationship" concerned.

Parsons,[43] discussing the social system, uses the case of medical practice as illustrative of a subsystem. In America there are certain expectations regarding the sick role. The patient is exempted from normal responsibilities of his social role, not held morally responsible for being ill, obligated to try to get well as promptly as possible and also forced to seek technically competent help. One of the layman's most serious problems is his lack of qualification to judge technical competence; this, together with his helplessness and the emotional disturbance usually accompanying illness, make him peculiarly vulnerable to exploitation. The social role of the physician demands that he place his patient's welfare first, and that he have access to the patient's body and confidence not granted in the same way to others, in return for which he is barred from taking advantage of these intimacies. There is much uncertainty in the results that the physician may hope to accomplish by his treatment, unlike the engineer, who can predict his results with considerable accuracy, even in the individual case. There is also the problem of transference, by no means restricted to psychiatrists. In fact, "the strains existing on *both* sides of the doctor-patient relationship are such that we must expect to find, not merely institutionalization of the roles, but special mechanisms of social control in operation."

Several studies of particular interest to physicians have been carried out. Dichter[44] made searching comments after analyzing the doctor-patient relation for the California Medical Society:

> The doctor is an integral part of the community and culture within which he lives. This culture and the people who are part of it are constantly changing . . . the change is positive . . . from immaturity and isolation to co-operation and participation . . . changes are slow . . . full of difficulties, slow downs and psychological sit-down strikes. . . .
>
> The modern doctor has lost his former position of community leadership which he used to share with the parish priest or minister and the teacher, because "a wrong turn was taken." [Doctors interviewed] felt as if they were being driven rather than being the drivers. They felt in general insecure, and behaved in many instances emotionally and immaturely.
>
> In a sense they had sold their birthright to leadership by shrugging their shoulders over the deplorable state of the world. Doctors, like everyone else, are like swimmers in a fast moving current. There are two ways to feel secure and to adjust oneself in such an ever-changing and progressing stream. One is to reach for a limb hanging from the shore and to find security by hanging onto it. The other is to swim along with vigorous movements in the general direction of the river of life.

Dichter found that patients are expecting a great deal more guidance from physicians than they are actually receiving, especially about community facilities for health and welfare services. The same idea was expressed in answers to questionnaires sent to community leaders in preparation for a recent conference on teaching psychiatry to medical students.[45]

Hall,[11] who has also studied the medical profession, came to the following conclusion:

> Specialized medicine is no longer an independent profession — a free lance occupation. It has become highly interdependent rather than independent, and is carried on within the framework of elaborate social machinery rather than within a freely competitive milieu. The main contingencies of a medical career hinge on the role which the doctor plays in a very complex, informal organization.

In such an organization the established members of the profession function "to provide order, to ascribe and maintain status, to control the conduct of members, and to minimize competition and conflict." Hall describes three types of physicians: the colleague type, closely identified with medical institutions of the community; the individualistic type, keenly competitive for patients and fees; and the friendly type, with an intense loyalty to persons rather than to institutions.

Caudill,[8] in his excellent summary of current research in the social sciences with medical implications, describes studies of the social structure of hospitals, which students of primitive society are apparently finding much more esoteric than they had expected, and a great many other interesting projects.

Anthropology

Anthropology, "which includes ethnology, archaeology and primitive linguistics, studies the races of men and their physical characteristics; the numerous widely varying human cultures scattered over the earth; and the ways in which different cultures interact upon being brought into contact or combination."[12]

Linton[46] speaks of anthropology as a science that "has concentrated its interest upon a single organism, man, and has tried to understand all sorts of phenomena as they affected him . . . the first of a series of synthesizing sciences the need for which is becoming ever more apparent."

The work of physical anthropology is not germane to this discussion, except for the point that though certain races of the world can be distinguished, the borderlines become very indistinct, and that[47] "biologically there are no fundamental physical differences in all stocks and all races . . . [and] biogenetic potentials are shared equally by all stocks and all races." Davis[48] remarks that "if one wishes to know what we may expect of a man, one needs to know in what kind of a culture, not in what race, he has been reared." Boyd[49] proposes a classification involving six major races, based on

blood groups, as being the only genetic factors known at present that do not shade imperceptibly from one race into another.

Cultural or social anthropology is more definitely a social science. Kluckhohn,[50] author of a readable popular book describing the work of anthropologists, says "Anthropology holds up a great mirror to man and lets him look at himself in his infinite variety."

Medicine in primitive cultures has been studied intensively by relatively few anthropologists. Clements[51] has pointed out that recurrent concepts of disease origin among primitive peoples include sorcery, breach of taboo, object intrusion, spirit intrusion and soul loss.

Ackerknecht[52] discusses the theoretical problem of primitive medicine very effectively:

> *There is primarily not one "primitive medicine" but there are numerous different primitive medicines. . . . The differences between primitive medicines are much less differences in "elements"* (they have a lot of common elements), *than differences in the medical "pattern"* which they build up and *which is conditioned fundamentally by their cultural pattern.* There is no inevitable position which illness and the healing art must take in society. . . . Medicine in primitive society is incidentally part of the spiritual section which often seems more conservative than the purely technical.

He also says[53]:

> Our medicine is not *the medicine* nor our religion *the religion* . . . primitive medicine is not a queer collection of errors and superstitions, but a number of living unities in living cultural patterns, quite able to function through the centuries in spite of their fundamental differences from our pattern . . . primitive medicine is essentially magic medicine . . . illness, like death or an accident, is generally not regarded by the primitive as a natural event. It is the consequence of supernatural actions or forces.
>
> The medicine man is a soul doctor and his fellow primitive whom we know as an emotionalist needs him badly . . . he gives peace by confessing his patient. His rigid system, which ignores doubt, dispels fear, restores confidence and inspires hope.

Ackerknecht gives several reasons for the not inconsiderable success of primitive medicine: it employs effective procedures, such as massage, baths, surgery and inoculation; it uses certain effective drugs, such as opium, cinchona, coca and laxatives; it practices psychotherapy, perhaps more effectively than the psychiatrist; it tends to maintain established social institutions; and it satisfies man's metaphysical craving.

Simmons,[54] who has recently been working at the Cornell-New York Hospital Medical Center, cites Elkin's[55] description:

> Aboriginal medicine men are far from being rogues, charlatans or ignoramuses. They are men of high degree . . . men who have undergone tests and have taken degrees in the secrets of life much beyond that which ordinary men have a chance to learn. This training involves steps which imply discipline, mental effort, courage and perseverance. In addition, they are men of respected, and often of outstanding personality. Thus they are of immense social significance, with the health of the group depending largely on faith in their powers. Furthermore, the various psychic powers attributed to them must not be readily dismissed as mere "make-believe," for many of them have specialized in the workings of the human mind and in the influence of mind on mind and mind on body. And, what is more, they are deeply convinced of their powers, so much so, that as long as they observe the customary discipline of their "order," their professional status and practice continues to be a source of faith and healing power to both themselves and their fellows.

Taylor[56] presents an interesting discussion of this problem, dealing with conflicts between Western medicine and "primitive" Hindu medicine.

Crew,[57] professor of social medicine in Edinburgh, holds that "the shape of medicine in the past has ever been a reflection of the shape of the society of which it was a part." Sigerist,[58] long concerned with the social and historical aspects of medicine, believes that the place of medicine in a society is determined by the current social and economic structure, the valuation that society places on health and disease, the tasks assigned to its physicians and the technology of medicine available to doctors at the time. At the time of Hippocrates physicians were itinerant craftsmen, rather low in the social scale. During the Middle Ages they tended to be clerics who "could practice medicine as a divine mission or as a charitable service" and had rather elevated social positions.

Cultural anthropologists were very useful during World War II. Mead[59] studied the food habits of various groups in the population, and proposed methods by which they might be altered to fit in more nearly with the rationing program. Leighton[60] made interesting studies of the Nisei Japanese moved from the West Coast to inland relocation camps, and worked out methods of dealing with their problems that would have been impossible without technics of understanding of their cultural background and psychology. Knowledge of the people in various occupied areas was of great benefit in administration of their affairs. Also, since the war, programs of technical health assistance[61] to foreign countries have been aided in numerous areas by anthropologic advice, and the World Health Organization has had an anthropologist on its staff.

Social Psychology

The following definition of social psychology has been given: ". . . in combination with psychology, sociology becomes social psychology, which is concerned with the mental processes and reactions of men in groups or masses."[12]

Miller[62] notes that "psychology has employed precise techniques more extensively than any of the other social disciplines." Improved methods of measurement and observation that have greatly facilitated new work include apparatus and sociometric devices to measure flow of social interaction; advances in sound recording; one-way vision glass for use in observation rooms; improvements in technics of interviewing and in using

questionnaires and polling methods; and procedures of scaling to quantitate attitudes.[63]

Current investigation in a number of interesting fields was discussed at the University of Chicago by Lippitt[10] and others[62] in 1947. The psychologic need for participation has been ably presented by Allport,[64] who holds that:

> . . . people must have a hand in saving themselves; they cannot and will not be saved from the outside. . . .
>
> . . . a balanced personality needs deep-rooted participation in all or most of the six spheres of value: the political, economic, recreational, religious, cultural-scientific and domestic. . . .
>
> . . . people have to be active in order to learn, in order to store up efficient memories, to build voluntary control, to be cured when they are ill, restored when they are faint. . . .
>
> . . . The individual's desire for personal status is apparently insatiable. . . .
>
> . . . when the work situation in which the individual finds himself realistically engages the status-seeking motive, when the individual is busily engaged in using his talents, understanding his work, and having pleasant social relations with foreman and worker, then he is, as the saying goes, "identified" with his job. He likes his work, he is absorbed in it, he is productive. . . .
>
> When, on the other hand . . . the individual goes through motions that he does not find meaningful, when he does not really participate, then comes rebellion against authority, complaints, griping, gossip, rumor, scape-goating disaffection of all sorts.

Elements that tend to produce favorable results are: "Friendly, unaffected social relations . . . consultation on personal problems . . . group decision . . . retraining of leaders according to democratic standards . . . face to face association." Mayo,[65] Roethlisberger,[66] Barnard[67, 68] and others have made similar points on the basis of their work in industry, also showing the great importance of informal groups among employees in controlling productivity.

Motivations and attitudes are becoming better understood through the use of projective material.[69]

The dynamics of groups have undergone intensive study, sparked by Lewin[70, 71] up to the time of his death and described in popular form by Chase[72] and more technically by Homans.[73] Dynamics of committees and professional conferences are becoming much better understood; leadership here as in other group situations is vital, and many of its important elements are being unraveled. Group therapy in psychiatry not only may prove a method of extending the services of psychiatrists, but also may actually be more effective than individual therapy in many types of cases.[74, 75] Alcoholics Anonymous, recipient of a recent Lasker Award in Public Health, is an outstanding example of group therapy without close professional supervision. There is some indication that obesity[76] can be successfully controlled in certain types of patients by similar technics. The morale of large groups was studied in the strategic-bombing surveys of Germany and of Japan,[77] and the studies of Stouffer et al.[78,79] on the American soldier have been called the greatest contribution of the social sciences since World War II.

Psychologic methods of testing are familiar to all concerned with medical-school admission, and they play important roles in all types of personnel work. Objective-type tests are being used more and more.[80] Selection methods used by the Office of Strategic Services[81] and the Air Force are especially interesting.

Psychologic problems of minority groups[82] have had a great deal of attention, one idea advanced being that the Negro's striving to better his condition in the midst of an unfavorable environment accounts for his high prevalence of hypertension — though this rate is not entirely confirmed. Barrabee, at the Boston Psychopathic Hospital, is studying the mental reactions of various ethnic groups in American culture as they appear in a mental-hospital population.

Lazarsfeld[83] and many others have contributed important findings to the dynamics of social communication as they are involved in mass mediums such as radio, and a number of rather complex technics are in use to determine the listening and "televiewing" habits of the public.

Psychologic motivation in economic behavior was intensively studied for the Treasury Department[84] during War Bond drives, and voting behavior is also being investigated.

The psychology of learning, basic to scientific health education, has come to be something of a football at present, with many theories being kicked about, and not too much common agreement on a theoretical basis. However, in a book discussing theories of learning, Hilgard[85] points out:

> The erroneous impression may be left that little is known about learning. The factual knowledge does in reality bulk large. . .. There is a common ground of understanding based upon an accepted logic of experimental inquiry and demonstrations, so that factual disagreements are readily arbitrated in the laboratory. Such disagreements over empirical fact as there are need not persist for long.

Health education of the public, referred to above, is often considered the responsibility of organized voluntary and official community agencies. Of course, it is also the physician's personal responsibility. He certainly should educate his patients and their families and do what he can as part of the community program. Health-education methods have changed materially in recent years, with much greater emphasis on community organization[86] and on helping the people to help themselves — a subject that has been well described by Hydrick[87] in what is now rural Indonesia and by Dodd[88] in Syria. Hydrick attempted "to awaken in the people a permanent interest in hygiene." He frankly says: "There would be no objection whatever to the use of coercion if its use could secure permanent results. But it has been tried so often without success."

Dent,[89] president of Dillard University, puts the modern philosophy of health education in the following terms:

> The goal of the modern health educator is *not* "to tell something *to* the people." Nor is it "to work out a solution *with* the people." His objective is *to help people work out their own solution to their public health problems.*

Economics

It has been stated that economics "examines the ways in which man obtains and uses goods and services."[12] So important has economics become to medicine that the American Medical Association has established a Council on Medical Economics, employing social scientists to analyze economic data of medical interest.

The use of index numbers to measure proportional changes in the costs of commodities or services as compared with a base period has become widespread, and is of obvious value. Business cycles have been intensively studied, those following Keynes' philosophy taking the view that governmental spending is needed in deflationary periods to prevent the panics of former years.

The prepayment-insurance principle for paying costs of sickness has become accepted, but the mounting costs of medical care still cause a great deal of concern, a commission on financing the costs of hospital care studying this aspect of the problem, and a presidential commission on the health needs of the nation also seeking a possible solution. There has been a great deal of interest in the British National Health Service,[90] and in what may be learned from it that may be helpful in the United States.

Social scientists have examined certain economic aspects of federal administration during World War II, from which useful lessons may be drawn.[91, 92]

Opportune investigation of an unplanned but controlled experiment in social economics is well described by McGonigle and Kirby[93] in a British community. It is summarized in the foreword as follows:

> A few years ago a population was transferred from slum dwellings to a modern self-contained housing estate, and kept intact without a mixture with other populations; there was also a second comparable population that continued to dwell in slum houses and served as a control. . . . Such favorable circumstances for human field research rarely occur. The expenditure and the health of these populations were carefully compared.
>
> Mortality rose in the group of families moved to new housing. Since they had to pay increased rent, expenditures for food were cut to a dangerously low level as most were unemployed and had extremely limited incomes.

Psychosomatic Medicine

In psychosomatic medicine, psychiatry and mental health, medicine and the social sciences have come so close together that they are shaking hands through the fence mentioned above. It is in this section of the medical field that social scientists feel most at home. And psychiatrists have found it easier than most other physicians to understand the methods and objectives of those working in social science, since psychiatrists must attempt to understand man's interpersonal relations and his total social environment as highly important to his disease manifestations.

Mead[94] believes that culture has been overlooked in the study of the dynamics of psychosomatic illness, the culture in which the physician himself and his colleagues grew up not being recognized as such but simply being considered "human nature" and therefore normal, with all other patterns falling into the category of deviations.

Halliday,[95] Goldston[96] and others have shown that psychosomatic disorders have greatly increased in recent decades because of environmental changes in a "sick society." According to Halliday, "during the present century, the trend of physical health steadily improved, whereas the trend of social health took an opposite direction." As characteristics of psychosomatic affections he states that "emotion is a precipitating factor, certain personality types are likely to be involved, the sex ratios are disproportionate, other psychosomatic affections are likely to be associated with the one producing presenting symptoms, there is likely to be a family history of similar disorders, the manifestations are phasic, and the 'prevalence is related to changes in the communal environment considered psychologically and socially.' "

Beale and his associates[97] recently reported a study of the records of 739 patients with stress diseases analyzed to determine the factors in personal adjustment to life situations that correlated best with degree of clinical improvement. A numerical rating scale that was developed has proved useful in prognosis.

Dunbar's[98,99] books have many basic references in the field. Schneider[100] reported that the emotionally upset soldier reported "sick" with types of disability — rheumatic, asthenic, gastrointestinal — that were acceptable to his group as originating through no fault of his own but nevertheless provided a relatively nonpunishing escape for him from a psychologically intolerable situation. During World War II the high incidence of so-called effort syndrome reported in World War I was not duplicated. Hysteria among women is also no longer commonplace. Both these types of behavior have now become so much more generally understood by a large segment of the people that they no longer offer the refuge formerly available.

As the field of mental health has developed, it is increasingly apparent that the psychiatrist alone cannot hope to provide the environment necessary for the most complete realization of personality possibilities that the mental hygienist sets as his goal. Many others who come in closest contact with the developing personality at its most crucial periods must play their essential roles, perhaps with guidance from the psychiatrist, who has the basic theo-

retical conception. Parents, teachers, ministers, social workers, public-health nurses and those who deal with delinquency and crime, as well as the family physician and many others, must work together with common understanding and a common goal to provide a community environment conducive to the best mental health of the individuals residing therein.

The National Institute of Mental Health, recognizing their importance to its field, is supporting a number of investigations in the social sciences.[101] The Commonwealth Fund,[102] long interested in mental health, sponsored an institute for psychiatrists and public-health officers to work out methods by which the principles of mental health might be applied more fully in public-health work. Previously, a somewhat similar institute for general practitioners and psychiatrists had been held.

The Grant Foundation is supporting a multidisciplinary community mental-health project in co-operation with the Harvard School of Public Health designed to work out ways of applying mental-health principles to the community as a whole, and the National Institute of Mental Health is conducting a similar multi-disciplinary project including social scientists in Arizona. Neither of these projects has yet submitted its final report.

Stanton and Schwartz,[103] also working on a multidisciplinary basis, have made intensive studies of patient-nurse-doctor involvement on psychiatric wards, showing that the informal relations that develop may be of great importance, and that when staff psychiatrists disagree about proper treatment of the patient, the patient has most unfortunate reactions.

A member of one research team actually became a patient on a psychiatric ward[104] to study the social interactions of patients, nurses and psychiatrists.

Integration of the Social Sciences with Disciplines Employed in Health Work

Social Medicine

The terminology used in medical approaches to the social sciences tends to be confusing. One might expect the term "social medicine" to be in general use to designate the aspects of medicine in relation to the social sciences. On the contrary, Halliday[95] says that social medicine "has a very floating meaning at present, being used in Europe as a synonym for staté-controlled medicine and in Britain as an alternative to preventive medicine in all its aspects." Grotjahn,[105] one of the foremost exponents of the subject in Germany, stated that since Bismarck's day the term had been used with reference to insurance medicine. Sand,[23] a prominent Belgian, however, favors the term social medicine.

Ryle,[106, 107] at Oxford, occupied the first of several chairs of social medicine recently established in the United Kingdon. He described the field as follows:

> . . . medicine applied to the service of man as *socius*, as fellow or comrade, . . . with a view to a better understanding and more durable assistance of all his main and contributory troubles which are inimical to active health and not merely to removing or alleviating a present pathology. It also embodies the idea of medicine applied in the service of *societas*, or the community of men, with a view to lowering the incidence of all preventable diseases and raising the general level of human fitness.

In the United States the Milbank Memorial Fund[108] and the New York Academy of Medicine[109] have sponsored symposia on social medicine, and Rosen[110] presents an excellent review of the subject. It is perhaps fair to say, however, that in the United States the term "socialized medicine" has been used so widely and so loosely that attempts to use "social medicine" to describe an intellectual discipline would be doomed to failure. This is unfortunate, since the term is concise and meaningful.

It is highly important to find more effective means to make collaboration easier between social scientists and health workers. The two groups tend to divide the same field in different ways because of their different backgrounds and concepts. A recent conference held by the University of North Carolina Division of Health Affairs dealt with these interrelations under the headings of social physiology, social epidemiology, psychosomatic medicine and general administrative problems. This grouping has the merit of permitting integration of data and concepts from the social sciences with existent disciplines already recognized by medical workers. The terms "social physiology" and "social epidemiology" require some explanation.

Social physiology deals with *individual differences*—their origins; how they are affected by the physical environment, including climate and altitude, and by the mode of life, including physical activity, diet, family situation, recreation and occupation; their role in the maintenance of health or the subsequent development of disease (especially degenerative and metabolic disease); and their effect on productivity.

Social epidemiology concerns identification and study of specific social factors in the occurrence of disease and mortality, as well as groups subject to special risk of disease and development and evaluation of technics for measuring health and detecting disease. Much of the work going on in departments of social medicine in the United Kingdom at present would come under this heading.

Epidemiology should be thought of in its etymologic meaning, as dealing with problems that are "upon the people," including those of acute communicable disease, but by no means limited to them. Gordon and his associates[111-114] and Clark and Morsell[115] have done much to extend the sphere of epidemiology as a method of inquiring into the

multiple causation of health problems of manifold type, including accidents, nutrition, mental health and high blood pressure. Epidemiology considers health problems as they result from the total interaction of the triad made up of the human host, the agent that directly produces the disease or injury and the environment in which both host and agent operate. In most conditions all three factors are operative, though in some the agent plays a predominant role and in others the host and again the environment. All three factors must be studied in the effort to arrive at a concept of the natural history of the problem so that a control program may be planned.

Problems in the Social Sciences

For a number of reasons, there has been resistance against the social sciences. They are relatively new, and innovations tend to be resisted. Linton[46] says: "it usually takes about a generation for the new discoveries and techniques of one science to become a part of the regular working equipment of other sciences." This lag is notable where social sciences are concerned. Social-science research takes time and is expensive, and findings are not easily demonstrable to those unfamiliar with the technical language and methods. Results of research are apt to carry obvious implications for social change, naturally resisted by vested interests. The multidisciplinary teamwork urgently needed for many investigations is difficult to bring about successfully.[116-120] There are some divisions among the ranks of the social scientists themselves, and the field needs a more unified approach and a broad theoretical concept upon which further research may be based. Efforts toward this unified approach are bearing fruit, such as the formation of the Department of Social Relations at Harvard, which combines sociology, social anthropology, social psychology and clinical psychology. Murray[121] says that "The plain truth is that we are in process of forming a new discipline, basic social science." Parsons and his associates,[122] Kluckhohn and Murray,[123] a group of social scientists assembled by the Viking Fund,[124] and many others are working toward the development of the much-needed broad theoretical concepts.

Another difficulty, noted by Lombard,[125] is that "In the social sciences, the sensitiveness of the phenomena being studied to the presence of an investigator is especially great." Leighton[126] makes a similar point: ". . . The man or woman who analyzes human relations is himself in the midst of human relations and a part of his society and culture" — that is, such a person is somewhat like a microbiologist who might find himself in the test tube as one of the bacteria he was studying.

Argument has been heated on the question of whether the social sciences are really "scientific" in the sense that some aspects of medicine are certainly scientific. Conant[127] and Barnard[128] have discussed this problem, and they agree that many of those studying human relations and behavior are genuine scientists.

The situation of the social sciences themselves is somewhat different. Barnard defines *a* science as: ". . . a substantial or relatively 'dense' body of knowledge: 1) validated in general by criteria accepted by the relevant group of scientists; 2) in general interconnected and self-consistent; 3) integrated by a theory or theories accepted by most scientists of the time as useful for further development of knowledge and its communication; and 4) associated with a living, active group of scientists who use it."

In this conception he does "not think there are as yet any social sciences." Both Barnard and Conant consider the field known as the social sciences as an admixture of true scientists — social philosophers, who, as Conant says, "are preparing the ground for the future social scientists in a fashion comparable to the work of the early philosophers in regard to natural phenomena"— and men of affairs who make investigations for purposes of planning or decision.

Despite all the difficulties, Cameron[45] makes the following point:

> Within recent decades, progress has been made in the scientific study of *human ecology* (the interaction of human organism with human environment), and of *personality* (the characteristics of human organisms resulting from this interaction) which compares favorably with the progress of physiology during the nineteenth and early twentieth centuries. There has gradually emerged out of the empirical, experimental and field studies in anthropology, psychology and sociology, a large and systematized body of knowledge which is steadily growing. Investigative techniques, likewise, have been developed which are appropriate . . . .

Marquis[129] modestly notes that ". . . traditional social sciences have developed as a mixture of common sense, speculative philosophy, historical scholarship, religion, wise advice, and some science." He discusses the scientific method, which has proved so fruitful in the natural-science field, and points out where the various social sciences have fallen short in the past.

Stouffer[130] and others have stressed the value of carefully designed social-science investigations using comparable control and experimental groups whenever possible.

Many today would agree with Kurt Lewin,[131] who said, "I am persuaded that it is possible to undertake experiments in sociology which have as much right to be called scientific experiments as those in physics and chemistry."

Applied workers in social sciences are badly needed:

> . . . skilled practitioners who can use social data for the cure of social ills as doctors use scientific data to cure bodily ills. At the moment the market can absorb many more trained social technicians than the universities are prepared to furnish.[132]

Medical social workers represent one group of such applied workers familiar to physicians, recently discussed by Ida M. Cannon.[133] The medical social worker is, however, in rather an anomalous position. Plant[4] has described it thus:

> The medical social worker stands in the same relation to the medical profession as does the probation officer to the courts — as an individual operating under a social philosophy totally different from that of those with whom she has to work . . . she may use her position to educate the medical group slowly to the fact that persons are more than bundles of interesting viscera, that they bring to the operating table all the triumph and defeat, the magnificence or tawdry cheapness of their streets and neighborhoods.

Medical educators are seeing the importance of training in the social factors of illness, and many medical schools have arrangements for students actually to see the patient's home and occupational environment, and to study its relation to his health or his illness.[134, 135]

Conclusions

Although material efficiency and physical-disease rates have improved in the past fifty years, the problems of working together in a complex society have increased. Psychosomatic disorders have likewise increased. Medicine needs the help of social scientists in solving the problems of a "sick society."

One may well say, with Sydenstricker, that "What is needed is more knowledge, dispassionately collected and scientifically analyzed with a wholesome respect for the complexities of human society and of the individuals who compose it, to form a sound basis for the conscious control of our destinies." Workers in the social-science field are realizing the value of the scientific method in carrying on their investigations, are becoming interested in health problems and are making important contributions.

References

1. Lissner, W. Shift in income distribution is reducing poverty in United States. *New York Times*, March 5, 1952.
2. Ruesch, J. Social technique, social status, and social change in illness. In Kluckhohn, K., and Murray, H. *Personality in Nature, Society and Culture.* 561 pp. New York: A. Knopf, 1948. Pp. 117-130.
3. Robinson, G. C. *The Patient as a Person: A study of the social aspects of illness.* 423 pp. New York: Commonwealth Fund, 1939.
4. Plant, J. S. *Personality and the Cultural Pattern.* 432 pp. New York: Commonwealth Fund, 1937. P. 43.
5. Bluestone, E. M. Medical care: community plan. *The Survey* **85**: 157-159, 1945.
6. Cherkasky, M. Montefiore Hospital home care plan. *Am. J. Pub. Health* **39**:163-166, 1949.
7. Sydenstricker, E. *Health and Environment.* 217 pp. New York: McGraw-Hill, 1933. Pp. 14 and 15.
8. Caudill, W. *Applied Anthropology in Medicine: An inventory of modern anthropology.* Wrenner-Gren Foundation, 1952. (Unpublished data.)
9. Health Information Foundation. *An Inventory of Social and Economic Research in Health, 1952.* 197 pp. New York: Health Information Foundation, 1952.
10. Lippitt, R. Strategy of sociopsychological research. In *Experiments in Social Process: A symposium on social psychology.* Edited by J. G. Miller. 205 pp. New York: McGraw-Hill, 1950. Pp. 17-30.
11. Hall, O. Sociological research in field of medicine: progress and prospects. *Am. Sociol. Rev.* **16**:639-644, 1951. Stages of medical career. *Am. J. Sociol.* **53**:327-336, 1948. Informal organization of medical profession. *Canad. J. Econ. & Polit. Sc.* **12**:30-44, 1946. Types of medical careers. *Am. J. Sociol.* **55**: 243-253, 1949.
12. Russell Sage Foundation. *Effective Use of Social Science Research in he Federal Services.* 47 pp. New York: Russell Sage Foundation, 1950.
13. Puffer, R. Industrial and occupational environment and health. *Milbank Mem. Fund Quart.* **26**:22-40, 1948.
14. Daric, J. Mortality, occupation and socio-economic status. *Vital Statistics* — Special Reports — Selected Studies. Vol. 33, No. 10, Sept. 1941. National Office of Vital Statistics, Pub. Health Service, Federal Security Agency.
15. Collins, S. Sickness surveys. In Emerson, H. *Administrative Medicine.* 1007 pp. New York: Thomas Nelson & Sons, 1951. Pp. 511-535.
16. Turner, V. *Hagerstown Health Studies: An annotated bibliography.* Pub. H. Bibliog. Series No. 6. 38 pp. Washington: Government Printing Office, 1952.
17. Reed, L., and Williams, H. Unique nature of Eastern Health District studies and census surveys. *Baltimore Health News* **25**:57-62, 1948.
18. Myrdal, A. *Nation and Family: The Swedish experiment in democratic family and population policy.* 441 pp. London: Kegan Paul, Trench, Trubner and Co., Ltd., 1945.
19. Political and economic planning. In *Population Policy in Great Britain.* 227 pp. London: Political and Economic Planning, 1948.
20. Hackett, L. W. Public health reminiscences. *California's Health* **10**:9-12, 1952.
21. Dorn, H. Effect of public health developments upon population growth. *Ann. New York Acad. Sc.* **54**:742-749, 1952.
22. Sax, K. Population problems. In Linton, R. *The Science of Man in the World Crisis.* 532 pp. New York: Columbia Univ. Press, 1947. Pp. 258-281.
23. Sand, R. *The Advance to Social Medicine.* 655 pp. London and New York: Staples Press, 1952. P. 442.

23a. Chapin, F. *The Measurement of Social Status by Use of the Social Status Scale.* 16 pp. Minneapolis, Minnesota: University of Minnesota Press, 1933.

24. Warner, W., and Lunt, P. S. *The Social Life of a Modern Community.* Yankee City Series, Vol. 1. 460 pp. *The Status System of a Modern Community.* Vol. 2. 246 pp. New Haven: Yale University Press, 1941.
25. Warner, W., and Srole, L. *The Social Systems of American Ethnic Groups.* 318 pp. New Haven: Yale University Press, 1941.
26. Warner, W., Meeker, M., and Eells, K. *Social Class in America.* 274 pp. Chicago: Science Research Associates, 1949.
27. Warner, W., et al. *Democracy in Jonesville.* 313 pp. New York: Harper, 1949.
28. Warner, W., and Davis, A. Comparative study of American caste. In Thompson, E. *Race Relations and the Race Problem: A definition and analysis.* 338 pp. Durham: Duke University Press, 1939.
29. Pfautz, H., and Duncan, O. Critical evaluation of Warner's work in community stratification. *Am. Sociol. Rev.* **15**:205-215, 1950.
30. Kinsey, A., Pomeroy, W. B., and Martin, C. F. *Sexual Behavior in the Human Male.* 819 pp. Philadelphia: Saunders, 1948. Pp. 385 and 393.
31. Young, P. V. *Scientific Social Surveys and Research.* 621 pp. New York: Prentice-Hall, 1950. Pp. 492 and 493.
32. Dickinson, R. E. *City Region and Regionalism: A geographical contribution to human ecology.* 327 pp. New York: Oxford, 1947.
33. Davie, M. Pattern of urban growth. In *Studies in the Science of Society.* New Haven, 1937.
34. Green, H. Cultural areas in city of Cleveland. *Am. J. Sociol.* **38**: 356-367, 1932.
35. *Idem.* Use of census tracts in analysis of city health problems. *Am. J. Pub. Health* **37**:538-542, 1947.
36. Faris, R., and Dunham, H. *Mental Disorders in Urban Areas.* Chicago: University of Chicago Press, 1927.
37. Buell, B., et al. *Community Planning for Human Services.* 464 pp. New York: Columbia University Press, 1952.
38. Murdock, G. School administration and community. *School and Society* **75**:5-8, 1952.
39. Richardson, H. B. *Patients Have Families.* 408 pp. New York: Commonwealth Fund, 1945.
40. Simmons, L. W. Frame of reference for family research in problems of medical care. In *Research in Public Health: 1951 Annual Conference of the Milbank Memorial Fund 162-181.* 20 pp. New York: Milbank Memorial Fund, 1952.
41. *Idem.* Social participation of aged in different cultures. *Ann. Am. Acad. Polit. & Soc. Sc.* **279**:43-51, 1952.
42. Parsons, T. Professions and social structure. *Social Forces* **17**: 457-467, 1939.
43. *Idem. The Social System.* 575 pp. Glencoe, Illinois: The Free Press, 1951. Pp. 436 and 450.
44. Dichter, E. *A Psychological Study of the Doctor-Patient Relationship.* Submitted to the California Medical Association–Alameda County Medical Association. California Medical Association, 1950.
45. American Psychiatric Association. *Psychiatry and Medical Education: Report of the 1951 Conference on Psychiatric Education held at Cornell University, Ithaca, New York, June 21-27, 1951.* 164 pp. Washington: American Psychiatric Association, 1952.
46. Linton, R. *The Science of Man in the World Crisis.* 532 pp. New York: Columbia University Press, 1947. P. 5.
47. Krogman, W. Concept of race. Cited by Linton.[46]
48. Davis, A. Racial status and personality development. *Scientific Monthly* **17**:354-362, 1943.

49. Boyd, W. *Genetics and the Races of Man: An introduction to modern physical anthropology.* 453 pp. Boston: Little Brown, 1950.
50. Kluckhohn, C. *Mirror for Man: The relations of anthropology to modern life.* 313 pp. New York: McGraw-Hill, 1949. P. 11.
51. Clements, F. Primitive concepts of disease. *Univ. Calif. Am. Archae. Ethno.* **32**:185-252, 1932.
52. Ackerknecht, E. Primitive medicine and culture pattern. *Bull. Hist. Med.* **12**:545-574, 1942.
53. *Idem.* Problems of primitive medicine. *Bull. Hist. Med.* **11**:503-521, 1942.
54. Simmons, L. Relation between decline of anxiety-inducing and anxiety-resolving factors in deteriorating culture and its relevance to bodily disease. In *Life Stress and Bodily Disease.* Vol. 29. 1135 pp. Baltimore: Williams and Wilkins, 1950. Pp. 127-136.
55. Elkin, A. *Aboriginal Men of High Degree.* 148 pp. Sydney: Australasian Pub. Co., 1944.
56. Taylor, C. Hindu medicine and India's health. *Atlantic Monthly* **190**:38-42, 1952.
57. Crew, F. Social medicine as academic discipline. In Massey, A. *Modern Trends in Public Health.* 581 pp. New York: Hoeber, 1949. Pp. 46-79.
58. Sigerist, H. E. Place of physician in modern society. *Proc. Am. Philos. Soc.* **90**:275-279, 1946.
59. Mead, M. Problem of changing food habits. *Bull. Nat. Res. Council.* No. 108, 20-31.
60. Leighton, A. *The Governing of Men: General principles and recommendations based on experience at a Japanese relocation camp.* 404 pp. Princeton: Princeton University Press, 1945.
61. *A Cross-Cultural Anthropological Analysis of a Technical Aid Program.* Edited by G. Foster. 104 pp. Washington: Smithsonian Institute, 1951.
62. *Experiments in Social Process: A symposium on social psychology.* Edited by J. G. Miller. 205 pp. New York: McGraw-Hill, 1950.
63. Guttman, L. Basis for scaling qualitative data. *Am. Sociol. Rev.* **9**:139-150, 1944.
64. Allport, G. Psychology of participation. *Psychol. Rev.* **53**:117-132, 1945.
65. Mayo, E. *Social Problems of an Industrial Civilization.* 150 pp. Andover, Massachusetts: The Andover Press, 1945.
66. Roethlisberger, F. J. *Management and Morale.* 194 pp. Cambridge: Harvard University Press, 1949.
67. Barnard, C. *Functions of the Executive.* 334 pp. Cambridge: Harvard University Press, 1938.
68. *Idem. Organization and Management.* 244 pp. Cambridge: Harvard University Press, 1948.
69. Bell, J. E. *Projective Techniques: A dynamic approach to the study of the personality.* 533 pp. New York: Longmans, 1948.
70. Lewin, K., Lippitt, R., and White, R. Patterns of aggressive behavior in experimentally created "social climates." *J. Soc. Psychol.* **10**:271-299, 1939.
71. Lewin, K. Dynamics of group action. *Educational Leadership* **1**:195-200, 1944.
72. Chase, S. *Roads to Agreement: Successful methods in the science of human relations.* 250 pp. New York: Harper, 1951.
73. Homans, G. C. *The Human Group.* 484 pp. New York: Harcourt, Brace Co., 1950.
74. Slavson, S., et al. *Bibliography on Group Psychotherapy.* 24 pp. New York: American Group Therapy Association, 1950.
75. Terhune, W., and Dickenson, J. Progress in group psychotherapy. *New Eng. J. Med.* **239**:854-857, 1948.
76. Kanter, S. Group psychotherapy for obesity. Presented at meeting of the American Psychiatric Association, May, 1951.
77. United States Strategic Bombing Survey. Morale Division. *The Effects of Strategic Bombing on German Morale.* 2 vol. Washington: Government Printing Office, 1946-1947.
78. Stouffer, S., et al. *Studies in Social Psychology in World War II.* Vol. 1. *The American Soldier: Adjustment during army life.* 599 pp. Vol. 2. *The American Soldier: Combat and its aftermath.* 675 pp. Vol. 4. *Measurement and prediction.* 756 pp. Princeton: Princeton University Press, 1949.
79. Hovland, C. I., Lumsdaine, A., and Sheffield, F. D. *Studies in Social Psychology in World War II.* Vol. 3. *Experiments on Mass Communication.* 345 pp. Princeton: Princeton University Press, 1949.
80. Long, L. Principles and purpose of objective testing. *Proc. Ann. Conf. M. Educ.* Feb., 1951. Pp. 45-48.
81. U. S. Office of Strategic Services, Assessment Staff. *Assessment of Men: Selection of personnel for the Office of Strategic Services.* New York: Rinehart, 1948.
82. U. S. War Department. *Leadership of the Negro Soldier.* Army Service Forces Manual. M5.
83. Lazarsfeld, P. F., and Kendall, P. *Radio Listening in America.* 178 pp. New York: Prentice-Hall, Inc., 1948.
84. Cartwright, D. Survey research: psychological economics. In *Experiments in Social Process: A symposium on social psychology.* Edited by J. G. Miller. 205 pp. New York: McGraw-Hill, 1950. Pp. 47-64.
85. Hilgard, E. R. *Theories of Learning.* 409 pp. New York: Appleton-Century Crofts, 1948.
86. Paterson, R. G., and Roberts, B. J. *Community Health Education.* 346 pp. St. Louis: Mosby, 1951.
87. Hydrick, J. *Intensive Rural Hygiene Work in the Netherlands East Indies.* Netherlands and Netherlands East Indies Councils, Institute of Pacific Relations, 1942. (Original 1937.) Pp. 12, 21 and 22.
88. Dodd, S. Controlled experiment on rural hygiene in Syria. *Pub. Am. Univ. of Beirut, Soc. Sc. Series.* No. 7, 1934.
89. Dent, A. Help yourself to health. *World Health Organization Newsletter.* No. 5, May, 1952.
90. Clegg, H. Background to Britain's health service. *New Eng. J. Med.* **247**:435-439, 1952.
91. U. S. Civilian Production Administration, Bureau of Demobilization. *Industrial Mobilization for War, Historical Reports on War Administration. War Production Board General Study No. 1.* Washington: Government Printing Office, 1947.
92. U. S. Office of Price Administration. *Studies in Industrial Price Control. Historical Reports on War Administration, Office of Price Administration, General Publication No. 6.* Washington: Government Printing Office, 1947.
93. McGonigle, G., and Kirby, J. *Poverty and Public Health.* 278 pp. London: Gollancz, 1936.
94. Mead, M. Concept of culture and psychosomatic approach. *Psychiatry* **10**:57-76, 1947.
95. Halliday, J. L. *Psychosocial Medicine: A study of the sick society.* 278 pp. New York: Norton, 1948.
96. Goldston, I. Social medicine and epidemic constitution. *Bull. Hist. Med.* **25**:8-21, 1951.
97. Beale, B., Pinsky, R., Wolf, S., and Wolff, H. Clinical guide to prognosis in stress diseases. *J. A. M. A.* **149**:1624-1628, 1952.
98. Dunbar, H. *Emotions and Bodily Changes.* Third edition. 604 pp. New York: Columbia University Press, 1946.
99. *Idem. Synopsis of Psychosomatic Diagnosis and Treatment.* 501 pp. St. Louis: Mosby, 1948.
100. Schneider, D. Social dynamics of physical disability in army basic training. *Psychiatry* **10**:323-333, 1947.
101. Clausen, J. Social science research in national mental health program. *Am. Soc. Rev.* **15**:402-409, 1950.
102. Ginsburg, E. L. *Public Health is People.* 241 pp. New York: Commonwealth Fund, 1950.
103. Stanton, A., and Schwartz, M. Management of type of institutional participation in mental illness. *Psychiatry* **12**:13-26, 1949.
104. Caudill, W., Redlich, F., Gilmore, H., and Brody, B. Social structure and interaction processes on psychiatric ward. *Am. J. Orthopsychiat.* **22**:314-334, 1952.
105. Grotjahn, A. Cited by Rosen.[110]
106. Ryle, J. A. Social medicine: its meaning and scope. *Brit. M. J.* **2**:633, 1943.
107. *Idem.* Social medicine: its meaning and its scope. *Milbank Mem. Fund Quart.* **22**:58, 1944.
108. Milbank Memorial Fund. *Backgrounds of Social Medicine.* 202 pp. New York: Milbank Memorial Fund, 1949.
109. *Social Medicine: Its derivations and objectives.* Edited by I. Goldston. 294 pp. New York: Commonwealth Fund, 1949.
110. Rosen, G. What is social medicine? Genetic analysis of concept. *Bull. Hist. Med.* **21**:674-733, 1947.
111. Gordon, J. Epidemiology of accidents. *Am. J. Pub. Health* **39**:504, 1949.
112. Gordon, J., and LeRiche, H. Epidemiologic method applied to nutrition. *Am. J. M. Sc.* **219**:321-345, 1950.
113. Gordon, J., O'Rourke, E., Richardson, F., and Lindemann, E. Biological and social sciences in epidemiology of mental disorder. *Am. J. M. Sc.* **223**:316-343, 1952.
114. Gordon, J. History of American epidemiology. In *The Twentieth Century — Yesterday, Today, and Tomorrow* (1920). 190 pp. St. Louis: Mosby, 1952.
115. Clark, E. G., and Morsell, J. Epidemiologic approach to study of high blood pressure. *Am. J. Pub. Health* **42**:542-548, 1952.
116. Caudill, W., and Roberts, B. Pitfalls in organization of interdisciplinary research. *Human Org.* **10**:12-15, 1952.
117. Eaton, J., and Weil, R. Psychotherapeutic principles in social research. *Psychiatry* **14**:439-454, 1951.
118. Eaton, J. Social processes of professional teamwork. *Am. Sociol. Rev.* **16**:707-713, 1951.
119. Glock, C. Some implications of organization for social research. *Social Forces* **30**:129-134, 1951.
120. Lee, A. Individual and organizational research in sociology. *Am. Sociol. Rev.* **16**:701-707, 1951.
121. Murray, H. Research planning: few proposals. In *Culture and Personality. Proceedings of an Interdisciplinary Conference, Nov. 1947.* 219 pp. New York: Viking Fund, 1949. P. 209.
122. *Toward a General Theory of Action.* Edited by T. Parsons and E. Shils. 506 pp. Cambridge: Harvard University Press, 1951.
123. Kluckhohn, C., and Murray, H. A. *Personality in Nature, Society and Culture.* 561 pp. New York: Knopf, 1948.
124. *Culture and Personality.* Edited by S. Sargent and M. Smith. Proceedings of an Interdisciplinary Conference. 219 pp. New York: Viking Fund, 1949.
125. Lombard, G. Self-awareness and scientific method. *Science* **112**: 289-293, 1950.
126. Leighton, A. *Human Relations in a Changing World.* 354 pp. New York: Dutton, 1949. P. 136.
127. Conant, J. B. *On Understanding Science: An historical approach.* 145 pp. New Haven: Yale University Press, 1948.
128. Barnard, C. *The Rockefeller Foundation: A review for 1950 and 1951.* 123 pp. New York: Rockefeller Foundation, 1951.
129. Marquis, D. Scientific methodology in human relations. In *Experiments in Social Process: A symposium on social psychology.* Edited by J. G. Miller. 205 pp. New York: McGraw-Hill, 1950. Pp. 1-16.

130. Stouffer, S. Some observations on study design. *Am. J. Sociol.* 55: 355-361, 1950.
131. Lewin, K. *Resolving Social Conflicts: Selective papers on group.* 230 pp. New York: Harper, 1948.
132. Herring, P. Social sciences in modern society. *Social Science Research Council Items.* March, 1947. Pp. 5 and 6.
133. Cannon, I. *On the Social Frontier of Medicine.* 273 pp. Cambridge: Harvard University Press, 1952.
134. Joint Committee of the Association of American Medical Colleges and the American Association of Medical Social Workers. *Widening Horizons in Medical Education.* New York: Commonwealth Fund, 1948.
135. Rosenfeld, L., Crowther, B., and Ring, M. *Social and Preventive Method Content and Teaching Methods: An annotated bibliography prepared for the Conference on Preventive Medicine in Medical Schools.* Washington: Government Printing Office, 1952.

MEDICAL INTELLIGENCE

THE EFFECTS OF L-THYROXINE SODIUM ON NONTOXIC GOITER, ON MYXEDEMA AND ON THE THYROID UPTAKE OF RADIOACTIVE IODINE*

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SYNTHETIC thyroxine is apparently absorbed and physiologically active when ingested, although it has generally been used intravenously.[1-6] Clinical studies employing oral administration of l-thyroxine sodium have demonstrated its effectiveness in treating and maintaining athyreotic patients.[5, 6] The possible advantages inherent in a therapeutic agent of constant potency and composition have prompted further clinical evaluation of l-thyroxine sodium in patients with myxedema. In addition, we have studied the suppressive effect of l-thyroxine administration on the thyroid uptake of radioactive iodine, as well as its influence on the size of nontoxic goiters.

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METHODS

Uptakes of radioactive iodine were determined in 7 patients with nontoxic goiters before and after two to eight weeks of orally administered l-thyroxine sodium (Elthrin)** in daily doses of 0.1 to 0.2 mg. The percentage uptake of an oral dose, usually 50 microcuries, was determined at twenty-four hours by direct monitoring of the thyroid gland.[7]

The influence of l-thyroxine administration on the size of nontoxic goiters was studied in 13 patients treated for three to twelve weeks. Treatment was continued for at least eight weeks unless clinical response occurred earlier. Five patients had nodular goiters, and 8 had glands that were diffusely enlarged two or three times the normal size. The initial daily dose of l-thyroxine was 0.1 mg.; this was increased by 0.1 mg. every four weeks if there was no response.

TABLE 1. *Suppression of Uptake of Radioactive Iodine in Patients with Nontoxic Goiters by Treatment with l-Thyroxine Sodium.*

CASE NO.*	UPTAKE OF RADIOACTIVE IODINE†		MAXIMUM DAILY DOSE
	BEFORE TREATMENT	AFTER TREATMENT	
			mg.
1	39	7	0.2
2	51	18	0.1
3	38	5	0.2
4	25	10	0.1
5	48	13	0.3
6	44	16	0.2
7	48	16	0.2

*These 7 patients appear under different numbers in Tables 2 and 3.
†Percentage of administered dose taken up by thyroid gland in 24 hours.

Seven patients with previously untreated myxedema were given l-thyroxine sodium in daily doses of 0.05 to 0.1 mg., increments of 0.1 mg. being added when the therapeutic response to the preceding dose had stabilized, until a euthyroid state was attained. Three patients who had been euthyroid while taking thyroid extract were changed to l-thyroxine sodium in an initial ratio of 0.1 mg. of l-thyroxine to 0.06 gm. (1 gr.) of thyroid extract.

RESULTS

The uptakes of radioactive iodine were suppressed in all patients studied (Table 1).

In 1 of 5 patients with nodular goiter the mass disappeared. Three of the other 4 who showed no

**Kindly supplied by Smith, Kline and French Laboratories, Philadelphia. It is stated by the manufacturer that 0.1 mg. of Elthrin is equivalent to 0.06 gm. (1 gr.) of thyroid, *U. S. P.*, and contains 65 microgm. of iodine.

response were operated on after eight to twelve weeks of l-thyroxine administration (Table 2). Two of eight patients with diffuse nontoxic goiter responded to l-thyroxine, with a return of the thyroid gland to normal size, and in 4 the size of the goiter definitely diminished. Two patients showed no change (Table 3).

TABLE 2. *Treatment of Patients with Nodular Nontoxic Goiters with l-Thyroxine Sodium.*

Case No.	Age	Duration of Goiter	Length of Therapy	Maximum Dose	Result	Pathological Diagnosis
	yr.		wk.	mg.		
8	17	12 mo.	4	0.1	Goiter disappeared	—
9	39	?	8	0.2	No change	—
10	48	?	8	0.2	No change; operation.	Colloid goiter
11	28	5 yr.	8	0.2	No change; operation.	"Premalignant" goiter
12	27	12 mo.	12	0.2	No change; operation.	Hemorrhage into cyst

TABLE 3. *Treatment of Patients with Diffuse Nontoxic Goiters with l-Thyroxine Sodium.*

Result	Case No.	Age	Duration before Treatment	Length of Treatment	Maximum Daily Dose
		yr.		wk.	mg.
Goiter disappeared	13	14	7 mo.	3	0.1
	14	14	4 yr.	6	0.2
Goiter smaller	15	52	?	12	0.2
	16	40	?	10	0.2
	17	16	?	8	0.2
	18	40	?	8	0.2
No change	19	28	8 wk.	8	0.2
	20	15	12 wk.	12	0.2

It has been shown that thyroid hormone suppresses the uptake of radioactive iodine by the thyroid gland.[8-10] In this respect synthetic l-thyroxine is apparently comparable to the biologic extract.

Although the goiters in 7 of the patients with nontoxic goiter discussed above disappeared or definitely diminished, the limited number of cases treated does not permit any statistical evaluation of the efficacy of this form of treatment or the factors determining clinical response.

Although it is apparent that our data do not permit a complete comparison of l-thyroxine and thyroid in the treatment of myxedema, it is our impression that there is no significant difference in the rate of response to these agents. Several additional patients are now being treated with l-thyroxine, and their response is quite comparable to that seen with thyroid extract. Synthetic thyroxine offers the advantages of constant uniform strength and composition and greater stability.

TABLE 4. *Treatment of New Cases of Myxedema with l-Thyroxine Sodium.*

Case No.	Age	Uptake of Radioactive Iodine*	Original Basal Metabolic Rate	Duration of Symptoms	Occurrence of Myxedema	Interval before Patient Became Euthyroid	Maintenance Dose
	yr.		%			wk.	mg./day
21	41	10.0	-30	5 mo.	Spontaneous	8	0.2
22	32	5.0	-13	4 yr.	Spontaneous	8	0.2
23	43	2.5	-43	2 yr.	Spontaneous	4	0.2
24	22	6.0	-28	6 wk.	Postoperative	12	0.5
25	46	—	-30	3 mo.	Postoperative	6	0.3
26	51	5.0	-20	7 mo.	Postoperative	6	0.2
27	35	1.4	-38	?	Postoperative	3	0.2

*Percentage of uptake of radioactive iodine by thyroid gland in 24 hours.

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Seven patients with previously untreated myxedema became euthyroid while receiving l-thyroxine sodium. Six of these patients were clinically euthyroid in three to eight weeks and were so maintained on 0.2 to 0.3 mg. daily. One patient did not become euthyroid for twelve weeks and then required 0.5 mg. as daily maintenance therapy (Table 4). Two patients previously maintained on 0.12 gm. (2 gr.) of thyroid required 0.2 mg. of l-thyroxine. A third patient, who had received 0.2 gm. (3 gr.) of thyroid extract apparently required 0.5 mg. of l-thyroxine (Table 5).

TABLE 5. *Patients with Myxedema Changed from Thyroid to l-Thyroxine Sodium.*

Case No.	Age	Basal Metabolic Rate	Occurrence of Myxedema	Previous Daily Dose of Thyroid	Maintenance Dose of l-Thyroxine Sodium
	yr.	%		gm.	mg./day
28	29	-9	Postoperative	0.12	0.2
29	42	-14	Postoperative	0.2	0.5
30	39	0	Spontaneous	0.12	0.2

Discussion

The biologic activity of synthetic l-thyroxine is manifested first by the suppression of radioactive iodine uptake in euthyroid persons, secondly by the reduction in size of nontoxic goiters in some persons and thirdly by its ability to induce remissions in patients with myxedema.

Summary and Conclusions

The effects of treatment with l-thyroxine sodium were studied in 23 patients. Oral administration of l-thyroxine sodium is comparable in its effects to thyroid extract, as manifested by its suppressive action on the uptake of radioactive iodine by the normally functioning thyroid gland, its capacity to induce a reduction in the size of nontoxic goiters in some patients and its ability to restore and maintain the euthyroid state in patients with myxedema.

References

1. Thompson, W. O., Thompson, P. K., and Dickie, L. F. N. Monosodium thyroxine, desiccated thyroid and impure sodium salt of thyroxine, comparison of their effect when administered orally with effect of thyroxine injected intravenously in alkaline solution. *Arch. Int. Med.* **52**:576-592, 1933.
2. Thompson, W. O., Nadler, S. B., Taylor, S. G., II, and Thompson, P. K. Recent observations on thyroxine and allied compounds. *Proc. Soc. Exper. Biol. & Med.* **31**:1000, 1934.
3. Clayton, J. C., Free, A. A., Page, J. E., Somers, G. F., and Woollett, E. A. Absorption and excretion dl-thyroxine labelled with radioactive iodine. *Biochem. J.* **45**:20, 1949.
4. Monroe, R. A., and Turner, C. W. Oral effectiveness of d, l-thyroxine in crystalline, monosodium and disodium forms. *Am. J. Physiol.* **156**:381-386, 1949.
5. Hart, F. D., and Mclagen, N. F. Oral thyroxine in treatment of myxedema. *Brit. M. J.* **1**:512-518, 1950.
6. Rosenblum, I., and Salter, W. T. Response of human athyreotics to levorotatory thyroxine, administered orally. *Federation Proc.* **10**: 111, 1951.
7. Burrows, B. A., and Ross, J. F. Management of hyperthyroidism. *M. Clin. North America* **35**:1305-1321, 1951.
8. Greer, M. A. Effect on endogenous thyroid activity of feeding desiccated thyroid to normal human subjects. *New Eng. J. Med.* **244**: 385-390, 1951.
9. Keating, F. R., Jr., Haines, S. F., Power, M. H., and Williams, M. M. D. Radioiodine-accumulating function of human thyroid gland as diagnostic test in clinical medicine. *J. Clin. Endocrinol.* **10**: 1425-1464, 1950.
10. Perlmutter, M., Weisenfeld, S., Slater, S., and Wallace, E. Z. Study of mechanism of inhibition of thyroid gland induced by ingestion of thyroid substance. *J. Clin. Endocrinol.* **12**:208-227, 1952.

DOCTORS AFIELD

David Livingstone: Missionary, Physician and Explorer 1813–1873

Dana L. Farnsworth, M.D.*

DAVID LIVINGSTONE, physician, missionary and explorer, was one of those people who are fortunate enough to attain a high place in the esteem and affection of their contemporaries, not by following the conventional pattern of a physician's career, or even that of a missionary, but by striking out boldly into a new field of action. He did this in the face of incredible hardships, all sorts of dangers, both known and unknown, and with little regard for his own personal, commonplace satisfactions. As one looks back on his activities over the span of a century, it may be worth while to examine his motivations and see what made such heroic action possible.

It is obvious that he was a man of iron will, great determination and at times even downright stubbornness. He tended to look upon all his associates as his helpers from the start, or so some of them thought,[1] and this was quite naturally irritating to a number of his seniors. He was also entirely forthright in his criticism of others, and when this was directed toward the missionary activities in South Africa, when he first arrived on the scene in 1841, much ill will toward him was generated. But all these minor deficiencies of character were as nothing compared to the positive qualities in his make-up.

Livingstone's childhood was spent in the general area of Scotland that his ancestors had lived in for several generations. Intense poverty was the rule in his family, and when he was ten years of age he began work in a textile factory near Glasgow. His schedule for the next few years gives some indication of the kind of life he was capable of living later on. He rose shortly after 5 o'clock, began work at 6, quit at 8 in the evening with intervals for breakfast and dinner, and then went to evening school from 8 to 10. After that he studied until midnight or later if his mother permitted.[2] Latin and the reading of Latin authors was his "core curriculum." He read everything he could get his hands on except novels. His only recorded rebellion against his father, for which he received "his last application of the rod," followed his refusal to read a theological book in preference to scientific works and books of travel. When he later returned on his own accord to reading more interesting books on religion he was gratified to find "that religion and science were not hostile but friendly to each other."[3]

In his family strong religious feeling, a high standard of morality and good works went hand in hand. Very early, while still in his teens, he resolved that he would spend his life easing human misery, and first picked China as his mission field. This decision being made, he then decided that he would obtain a medical education to be better qualified for such work.

While he was completing his medical studies he became connected with the London Missionary Society and did enough work under the supervision of its officers to be ordained for the ministry in the same month in which he received his medical degree. Although officially a minister he never became a theologian in the formal sense.

By the time he was ready to go abroad the scene of his labors had been changed from China to Africa. Within a month of his graduation and ordination he was on his way to Cape Town, arriving there after an eighty-two-day voyage, only to find an unhappy state of affairs with the missionaries in that neighborhood. They were jealous and lacking in unity and energy, and had adopted various rationalizations for their self-protective course. He thought something was radically wrong with the missionary outlook and said so with enough vigor to earn unpopularity then and unwarranted criticism later.[4]

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His first period of activity in Africa being under the auspices of the London Missionary Society, was almost entirely in the spirit of the usual missionary enterprise — namely, to save as many souls as possible. He searched for a suitable station but found none that seemed to justify permanent settlement. He soon saw that only drastic action in opening up the whole southern continent would achieve rapid results. This course appealed to the explorer in him, but unfortunately he could not sell the idea to his sponsors. A friendly parting from the Society followed, and the British Government took up support of his work. At the time of his change of sponsorship he made the first of his two return visits to Great Britain, where he found himself a national hero.

Although what little support he got for his various expeditions after leaving the London Missionary Society was from governmental or personal private sources, he always considered himself a missionary and a virtual emissary of Christ in his attempts to open up the continent and subdue the slave trade. Almost every entry in his journals confirms this attitude. The hardships he encountered are almost unbelievable, even though they have become so well known as to be considered nearly in the class of folk-lore. His encounter with the lion, in which his left arm was crushed, leaving him with a false joint in the humerus, the troubles with hostile natives, the destruction of all his personal belongings by the Boers, the constant weariness, the ever-recurring malarial fevers, trypanosomiasis and dysentery, the death and burial of his wife in Africa in 1862 — all these make exciting reading, best appreciated in Livingstone's own direct and simple language in the *Journals*.[5, 6]

There is something of the essence of tragedy in the last years of this man, consumed by determination, discouraged by misunderstandings and lack of support, nearly dead at times from illness or starvation, the object of treachery as well as saint-like devotion by his native attendants, heart-broken at the loss of his wife, wandering around in deepest Africa. The removal of his body to London for final burial was the last in a whole series of fantastic happenings.

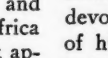
Though he could not live to know it fully, his was one of the most influential lives of the nineteenth century. His work as an explorer was of such caliber that no other person did so much toward an understanding of African geography as he did. He was a keen observer, skilled in describing in scientific terms the places, animals and plants that he saw. He kept meticulous records during all his travels. His influence and reputation made less difficult the travels of later visitors. In the face of the most frightening circumstances he repeatedly demonstrated utter fearlessness, especially when dealing with hostile natives.

Medicine was for him the means to an end, but he constantly tried to find the cause of the various fevers he encountered. In his journal he stated that "when our posterity shall have discovered what it is which, distinct from foul smells, causes fever . . .they will pity our dulness of perception." He noted that malaria was absent on heights, prevalent in swampy areas, and said that "myriads of mosquitoes showed, as probably they always do, the presence of malaria."[7] Yet he, like all others before Sir Ronald Ross, never bridged the gap to the concept of the mosquito as the actual carrier of the disease.

In what did his greatness consist? This quality is not a mold into which a capable man's life can be poured. Rather, it is a structure that can best be viewed objectively, probably even from a distance, so that minor imperfections do not obscure the outlines. Those who were close to Livingstone did appreciate his greatness for the most part, though as with Wo drow Wilson, some chose to emphasize his weaknesses. The grandeur and immensity of his concepts, together with his utter devotion to realizing them, constituted the core of his greatness. Elimination of the slave trade, linked with the opening up of a whole new continent, appealed to his religious as well as his exploring propensities and thus gave meaning to a life marked by prodigious industry and incredible hardship. The sacrifice of his own life added the necessary symbolic touch to make his name and deeds remembered with veneration wherever integrity and sincerity are beyond price.

References

1. Campbell, R. J. *Livingstone.* 295 pp. New York: Dodd, Mead & Co., 1930. P. 72.
2. Livingstone.[1] P. 3.
3. Ibid. P. 4.
4. Campbell.[1] P. 49.
5. Livingstone, D. *Missionary Travels and Researches in South Africa.* 687 pp. London: John Murray, 1857.
6. *Last Journals of David Livingstone.* Edited by H. Waller. 2 vol. 706 pp. London: John Murray, 1874.
7. Campbell.[1] P. 122.



CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 38491

PRESENTATION OF CASE

A sixty-three-year-old physician was admitted to the hospital because of diarrhea and dehydration.

Three days before entry the patient had been waked from a sound sleep by abdominal cramps, diarrhea and a chill. His wife stated that he had eaten nothing unusual and had seemed well until the sudden onset of symptoms. Fever developed, and the diarrhea became progressively worse. He was confused mentally, and on the morning of entry had become weaker and less responsive.

Two years prior to admission the patient retired because of heart disease. One year later he had a "coronary attack" and was hospitalized for a month. Since then he had led a quiet life, had been asymptomatic and had taken no medicine except aminophylline occasionally.

On physical examination the patient was confused and exhibited signs of high fever and dehydration. There were fine, moist rales at both lung bases. The heart was normal. There was no tenderness, muscle spasm or masses on abdominal examination. Peristalsis was reduced but present. The prostate was hypertrophic. The neck was not stiff.

The temperature was 104.7°F., the pulse 140, and the respirations 30. The blood pressure was 60 systolic, 40 diastolic.

The urine was cloudy, amber, acid, and not of sufficient quantity for a specific-gravity determination; it gave a + reaction for albumin and a ++ reaction for bile; the sediment contained 1 red cell, 15 white cells and a moderate number of bacteria per high-power field. The blood hemoglobin was 13.8 gm., and the white-cell count 27,300, with 92 per cent neutrophils, 5 per cent young neutrophils, 2 per cent lymphocytes and 1 per cent monocytes. An emergency blood sugar taken during glucose infusion was 270 mg. per 100 cc. The nonprotein nitrogen was 42 mg. per 100 cc., and the sodium was 130.8 milliequiv., the potassium 8.6 milliequiv., the chloride 92 milliequiv., and the carbon dioxide 15.9 milliequiv. per liter. An electrocardiogram showed a sinus tachycardia of 120, normal axis and a PR interval of 0.15 second. The T waves were upright in Leads AVL, V_2 and V_3, low and upright in Leads 1, V_1, V_4, V_5 and V_6, diphasic in Lead 2 and inverted in Leads 3 and AVF. The ST segment was slightly depressed in Lead 2. A single anteroposterior film of the chest taken with a portable machine was of poor quality and did not include all of the left lung. The right leaf of the diaphragm was somewhat elevated. There was a suggestion of some abnormal density at the right base and possibly some increase in pleural fluid on this side. The heart was probably somewhat enlarged.

Later on the day of admission cyanosis, dyspnea and sweating developed, and the patient was barely responsive after an attempt to get out of bed. The pulse was rapid and regular, and the heart sounds were of poor quality and very distant. He was placed on a regimen of streptomycin, penicillin, aureomycin, digitoxin, oxygen and intravenous injection of fluids. During the next sixteen hours the temperature dropped to 100°F., the pulse to 120, and the respirations to 20. The urinary output was scanty. On the second hospital day the patient had Cheyne-Stokes respirations and was comatose, but findings on physical examination were as before. There were no neurologic signs. The temperature again rose to 104°F., the pulse to 130, and the respirations to 30. The blood pressure was 108 systolic, 70 diastolic. During this twenty-four-hour period, the patient's fluid intake was 3000 cc., whereas his urinary output was only 240 cc. The urine was grossly bloody, had an alkaline reaction and gave a + test for albumin; the sediment contained countless red and white cells and a large number of bacteria. The white-cell count was 32,000, with 95 per cent neutrophils, 1 per cent young neutrophils, 2 per cent lymphocytes and 2 per cent monocytes. The blood sodium was 134.9 milliequiv., the chloride 101 milliequiv., the potassium 4.6 milliequiv., and the carbon dioxide 20.2 milliequiv. per liter. On the third hospital day the patient exhibited signs of increasing respiratory difficulty and was cyanotic and unresponsive. The breath sounds at the right-lung base were diminished, and more rhonchi were heard bilaterally. The abdomen was soft, without any localizing signs. On thoracentesis done through the ninth interspace in the right posterior axillary line, no fluid was obtained. Still later in the day the breathing became stertorous. The neck was stiff, and Kernig's sign was positive bilaterally. A lumbar puncture showed crystal-clear spinal fluid that was free of cells and had normal dynamics. Early on the fourth hospital day, the patient began to twist his head from side to side, shrugged his shoulders and arms several times, had a few gasping respirations and died.

Throughout the patient's hospital stay, the temperature ranged between 100 and 104°F. daily. The urinary output during the first hospital day was 145 cc., on the second 240 cc. and on the third 40 cc. He continued to have a large number of liquid stools.

Differential Diagnosis

Dr. Thomas Paine*: I do not propose to make anything complicated out of this case. Quite simply, this is the last chapter in the story of a sixty-three-year-old man who had been retired for a year because of a condition that sounds like a myocardial infarction and who contracted a severe infection associated with the picture of renal shutdown and then death. Old people and very young people are more susceptible to the ravaging effects of invading micro-organisms than people in between these extremes of age. I think that if a young man had had such a gastroenteritis as this man suffered he would probably not have had to turn in his ticket at the end of the run as the patient under discussion did. I am willing to accept the suggestion in the history that this patient did undergo a myocardial infarction one year before admission and that he entered his final illness with a heart that was able to meet the demands of a retired life but not that of mortal combat with pathogenic bacteria. The borderline position of his cardiac reserve was indicated by the history of taking aminophylline; this may have been for episodes of cardiac asthma.

The precipitating cause of the last illness seemed to be an acute enteritis. The patient was wakened from sleep by abdominal cramps, diarrhea and a chill. For the next three days he continued to have high, remittent fever associated with diarrhea. And then he entered the hospital with severe acidosis, dehydration and what, I suppose, might be termed "medical shock." This is the same picture that is seen when an infant enters the hospital with severe gastroenteritis; in such a case, however, the correction of the electrolyte disturbance is likely to be associated with recovery. This patient, though attempts to correct the electrolyte disturbance were partly successful as judged by the improvement in electrolyte values, did not recover.

The two organ systems that were mainly involved and that probably contributed most to the patient's death were the cardiac-circulatory and the urinary-tract systems. How and why did they deteriorate in the face of infection in the gastrointestinal tract? When the patient entered the hospital with gastroenteritis he was in shock, which could reasonably be accounted for by the loss of fluids and electrolytes from the gastrointestinal tract. This peripheral circulatory collapse with diminished circulating fluid volume can have a deleterious effect on many organ systems. If arteriosclerotic changes are already present in blood vessels, they are perhaps more likely to undergo thrombotic changes — for instance, in the central nervous system or in the coronary arteries.

The most sensitive organs to the effects of shock, however, are probably the kidneys, and in shock the reduction of renal blood flow is out of proportion to the reduction in cardiac output. The renal effects of shock may take the form of lower-nephron nephrosis, with resulting oliguria, anuria and uremia. This is a real possibility in the case under discussion. Another renal lesion associated with renal shutdown that may accompany severe infection is so-called bilateral cortical necrosis. This, however, is reputed to be rare in the absence of pregnancy. A third renal lesion — and one that I think most likely here — is pyelonephritis with necrotizing papillitis. The stage was set for this condition in that he had prostatic hypertrophy, with perhaps some previous obstruction to the urinary outflow. Bacteria were noted in the initial urine examination, and as the patient deteriorated, the urine became loaded with red cells, white cells and bacteria. Necrotizing papillitis, which is a severe form of pyelonephritis usually seen in diabetes, is occasionally seen in nondiabetic persons in whom it is usually associated with some element of urinary obstruction. In the past, Dr. Castleman has not been above subjecting persons in my present location to this particular pathological surprise.

Getting away from the kidneys for a few minutes, let us look at some of the other signs and symptoms that appeared while the patient was in the hospital. The electrocardiogram may have indicated an old posterior myocardial infarction; or were the changes described a result of the high blood potassium? I should like to have some help on the interpretation of the electrocardiogram.

Dr. Benjamin Castleman: I can read you the interpretation: "The tracing is abnormal. It suggests the possibility of an old posterior myocardial infarction. There is no definite evidence of recent myocardial infarction."

Dr. Paine: The x-ray film of the chest was described as showing an abnormal density at the right base and some fluid. May I see that film?

Dr. Joseph Hanelin: The quality of the film is so poor that not much can be said about it. Not all the left lung or the heart is on the film. The heart looks as though it might be large, but magnification is a factor in causing apparent enlargement here. The right leaf of the diaphragm seems slightly elevated; there appears to be a hazy density at the right base, and there may be some increase in fluid, but that is largely guesswork. The markings, which are visible on the left, appear prominent.

Dr. Paine: So he could have had infarction, tumor, pneumonia, atelectasis and so on?

Dr. Hanelin: That is correct.

*Assistant physician and chief of the bacteriology laboratory, Massachusetts General Hospital.

DR. PAINE: On the day of admission when he attempted to get out of bed, the patient became cyanotic, dyspneic, sweaty and unresponsive. I suppose that this picture could simply represent a more severe degree of the shock-like state, a pulmonary infarction or acute pulmonary edema secondary to a failing left side of the heart or acute pulmonary edema secondary to a new myocardial infarct. In any event the patient was given digitoxin, oxygen, antibiotics and fluids intravenously; despite these efforts, he lapsed into coma, the urinary output remaining small, and died approximately seven days after the beginning of the enteritis.

It seems to me that the death of the patient must have been caused by failure of the heart, by the severe infection or by a combination of these factors. The terminal episode could, I suppose, have been the result of a massive pulmonary embolus, which I see no way of ruling in or out, but in any event the stage had been set for pulmonary embolus by the cardiac failure and severe infection. The same thing might be said about a terminal myocardial infarction. Renal shutdown from whatever cause should not result in death in this short a period if the patient were not overhydrated — that is, if fluid intake was kept equivalent to fluid loss. But maintenance of the intake of fluids and electrolytes at the optimum level is difficult in any patient with renal shutdown; when to renal shutdown is added copious diarrhea, infection with high fever and a damaged heart, maintenance of the optimum level does indeed become logarithmically complicated.

It is my understanding that pertinent data are never purposefully omitted from these protocols. In any event I am curious about the so-called liquid stools. Did they contain shreds of mucus, blood or motile amebas?

DR. DANIEL S. ELLIS: No stools ever reached the laboratory because the patient was incontinent of feces, and the nursing staff did not think of obtaining a specimen from the sheets to send to the laboratory for culture.

DR. PAINE: Was there blood or mucus on the sheets after the water had evaporated?

DR. ELLIS: They were brown, watery stools with no other gross abnormality.

DR. PAINE: What was seen on Gram-stain smear of the urine?

DR. ELLIS: The bacteria were noted on routine examination of the urinary sediment.

DR. PAINE: What organisms were yielded on culture of the stool, blood and urine?

DR. ELLIS: We received no report of stool and blood cultures before the patient died. One urine culture the day before death showed *Escherichia coli*.

DR. PAINE: The severity of the enteritis in association with chills and high fever suggests that an organism of some virulence was at work — for instance, a salmonella. Organisms of a low degree of virulence, such as *Salmonella typhimurium*, tend to produce more gastroenteritis but less invasion of the blood stream than this patient exhibited. A very virulent salmonella, such as *S. choleraesuis*, tends to invade the blood stream, producing a more septic course and results in a higher mortality rate than *S. typhimurium*. When a salmonella invades the blood stream it may localize in the heart valves, in the central nervous system, in the bones or in the kidneys and may even produce a pyelonephritis. The high white-cell count, with the predominance of neutrophils, is against salmonella infection, which is usually accompanied by a leukopenia, with depression of the neutrophils.

Another organism that might be considered is the staphylococcus. One could visualize staphylococcal food poisoning with perhaps a spread of the organism into the blood stream from the gastrointestinal tract and localization of septic emboli in the kidneys, with an acute pyelonephritis and renal failure on that basis. But staphylococcal food poisoning usually does not result in such a protracted course of diarrhea. It tends to produce a severe gastroenteritis, with a shock-like state, low fever and rapid recovery.

Another possibility is acute bacillary dysentery due to a strain of shigella, but this organism usually does not cause a septicemia-like picture with such a high remittent fever. Perhaps this patient suffered from an enteritis of unknown etiology, similar to epidemic nausea, vomiting and diarrhea — syndromes that appear every year and are thought to be of viral etiology. Perhaps the accompanying shock-like state was associated with an activation of an asymptomatic urinary-tract infection, which progressed to the severity of a necrotizing papillitis. The entire septic course may have been primarily due to the severe renal infection.

Terminally the urine was described as containing a large number of bacteria and having an alkaline reaction. This suggests that the organism infecting the urinary tract may have been a proteus. The proteus organism is a bad actor, being quite resistant to antibiotics — penicillin, aureomycin, chloromycetin and terramycin; it may quickly become resistant to streptomycin. Perhaps the presence of a proteus would explain the lack of response to the chemotherapy that was given this patient. If there were organisms in this patient's blood stream, they could have localized anywhere in his body, including the lung, to give the shadow noted on the chest x-ray film, or in the brain, to give the stiff neck. But there is little other evidence to support these conjectures.

My final diagnoses, then, are pyelonephritis, with necrotizing papillitis, perhaps due to a proteus, congestive heart failure secondary to arteriosclerotic heart disease and old myocardial infarction,

enteritis of unknown etiology, at least to me, and prostatic hypertrophy.

A PHYSICIAN: Along with the pyelonephritis, do you think the patient had a Gram-negative septicemia?

DR. PAINE: He certainly could have had.

A PHYSICIAN: We have seen such patients pursue a similar course to that with septicemia due to *Esch. coli* from a primary infection in the urinary tract.

DR. PERRY J. CULVER: Do you think Weil's disease might be considered as an outside possibility here?

DR. PAINE: I do not think I should consider it strongly. I do not remember having seen enteritis of this sort in association with Weil's disease. Have you?

DR. CULVER: No; I raised the question because of the bile in the urine and the high white-cell count and hematuria later.

DR. PAINE: Bile was noted once and was not mentioned again.

DR. RAYMOND D. ADAMS: I wonder if one can altogether exonerate the central nervous system. The protocol says that there were no neurologic signs, but in my estimation coma is one. What is meant is that there were no lateralizing or focalizing neurologic signs. On admission this man was confused. That could be explained on the basis of either fever or circulatory collapse. When the blood-pressure level reaches 70 systolic, a patient in shock often is comatose, stuporous or confused. Yet on the next day the blood pressure was normal, but the coma remained deep. Another point is that the neck was said to have been stiff on the second day; I do not quite understand that.

DR. PAINE: Neither did I.

DR. ADAMS: One would expect the neck to have been supple if he was comatose from some general metabolic disturbance; however, if a decerebrate state or some space-taking lesion in the cranial cavity that tended to herniate the cerebellum had supervened, that would explain the stiff neck. Stiff neck may be due to meningitis, to increased intracranial pressure with brain herniation or to generalized muscular rigidity. I wonder if the disorder of the central nervous system might not have played an important part in this man's death. I also agree that the evidence favors an infection in the urinary tract with septicemia. This raises the question of abscess in the central nervous system, though the other findings do not support that diagnosis. I am unable to define the nature of the pathologic process within the central nervous system.

DR. CASTLEMAN: Would you describe the stiff neck as a meningismus such as is seen with pneumonia or other infections?

DR. ADAMS: The term meningismus is an unsatisfactory one; it has so many different meanings that we rarely use it any more. Certainly, in infections, particularly right-upper-lobe pneumonia, one sees stiff neck with a clear cerebrospinal fluid. This has been called meningismus. Some clinicians use the term to designate an aseptic (sympathetic) meningitis, in which there is pleocytosis and sometimes increased content of protein without bacteria or other organisms.

DR. CASTLEMAN: What is the cause of the stiff neck in such cases?

DR. ADAMS: It is not known.

DR. CASTLEMAN: Dr. Colby, have you any comment?

DR. FLETCHER H. COLBY: Dr. Paine has summed this case up brilliantly. Are not these central-nervous-system symptoms always found in patients with uremia?

DR. ADAMS: I do not think so; my impression of "nonhypertensive" uremia is that it seldom causes evidence of increased intracranial pressure, headache, focal neurologic signs, convulsions or stiff neck.

DR. PAINE: People with severe infection or severe cyanosis may be comatose and may have all sorts of decreased function of the brain nuclei. My assumption was that the coma was probably based on the severe infection along with the cyanosis secondary to the cardiac congestion. I cannot rule out the presence of something in the brain.

DR. ELLIS: I have only a few comments on the clinical picture. This patient, who was admitted on the surgical service one morning about 11:00 a.m. without previous notice, presented a real emergency but obviously not a surgical emergency. He was hot and flushed but very dry and was combative of any effort to move him. When I tried to draw blood from his arm, he resisted and thrashed around. When we spoke to him he did not answer but looked at us with a blank stare. His confusion had come on rapidly within the four hours before admission. In the history obtained from his wife the only symptom referable to the urinary tract was some difficulty in starting the stream and some nocturnal frequency. So far as we knew he had not complained of any burning or any other urinary symptoms. The illness seemed to have started with the acute diarrhea; it seemed to us that he had an acute infectious enteritis or enterocolitis.

We were puzzled and disturbed by the low blood pressure, the mental picture and the lack of response to therapy. He was not in acute peripheral vascular collapse; he was not cyanotic, cold or clammy at the time. He had hypotension. We thought we were dealing with infection and wondered about Addison's disease, with the low blood pressure and acute diarrhea. The only clue that the urinary tract was involved was the report of the + test for albumin and some bacteria in the urine. The urine was not grossly abnormal, until after the indwelling catheter had been inserted. This was done because

the patient was having some retention and we wanted to know about his fluid intake and output. That afternoon he became violent, thrashed about in bed and resisted all efforts to keep him there. At that time he had this acute episode of cyanosis and collapse. Thereafter, the urine became bloody. At first we thought the bloody urine was due to trauma from the indwelling Foley catheter. We believed that the cardiac episode was an acute coronary occlusion. By the next day, when he was no better and suddenly became worse, we thought we were dealing with a septicemia, probably originating in the gastrointestinal tract. The blood cultures were reported at the end of thirty-six hours as showing nothing. The stools at the end of thirty-six hours had not been sent to the laboratory. The day before he died we did get a telephone report that the urine culture showed colon bacilli. He was started on penicillin and streptomycin to cover things until we received the report of the blood culture. At the end of thirty-six hours when he did not improve he was put on intravenous injection of aureomycin and died thirty-six hours later.

I think the stiff neck was simply a resistance to any motion that the examiner tried to make rather than due to actual meningeal irritation. He had no other localizing or lateralizing neurologic signs.

Clinical Diagnoses

Bacteremia, cause undetermined.
Acute gastroenteritis.
Myocardial infarct, old.
Recent pulmonary infarct.

Dr. Paine's Diagnoses

Pyelonephritis, with necrotizing papillitis.
Congestive heart failure, secondary to arteriosclerotic heart disease and old myocardial infarction.
Enteritis of unknown etiology.
Prostatic hypertrophy.

Anatomical Diagnoses

Prostatic abscess.
Pyelonephritis and pyonephrosis, acute.
Septicemia, due to Esch. coli.
Acute brain purpura (pericapillary encephalorrhagia).
Myocardial infarct, old.

Pathological Discussion

Dr. Castleman: After the autopsy was performed we received a blood culture report of *Esch. coli*, and the cause of this man's death was septicemia due to the colon bacillus. The source of the infection as far as we can tell was not in the intestinal tract. The entire intestinal tract was carefully examined and showed no evidence of inflammation anywhere. This is not too surprising since even in infants with fever, diarrhea and infection, we do not find much on examination.

One of the kidneys was congenitally aplastic, measuring 2 by 3 by 1 cm. in size, and apparently had not worked for a number of years, if at all. The other kidney weighed over 400 gm. so that there had been a compensatory hypertrophy over the years. This enlarged kidney showed a severe pyelonephritis and pyonephrosis, with numerous abscesses through the kidney, not a necrotizing papillitis. The source of the infection was the prostate, which was boggy and enlarged, not because of hyperplasia but because of numerous abscesses. The urinary bladder at the time of autopsy was markedly infected as well. I think the prostatic abscesses led to the severe pyelonephritis, septicemia and death.

The heart showed an old posterior myocardial infarct and small foci of acute necrosis in the myocardium that were undoubtedly due to the septicemia. There was not a true myocardial infarction of recent origin but foci of early small abscesses.

The spleen was large and septic.

The brain at the time of autopsy did not look abnormal on the outside but apparently was on the inside. Perhaps Dr. Richardson will tell us about that.

Dr. Edward P. Richardson, Jr.: As Dr. Castleman mentioned, the brain before cutting was not in any way remarkable and gave no evidence whatsoever of meningitis. On section, we found a multitude of small hemorrhagic lesions, 2 mm. or less in diameter, scattered diffusely throughout the white matter of both hemispheres, in the corpus callosum (where there were a great many), in the midbrain and in the upper pons. The gray matter, on the other hand, was remarkably intact, and there were few if any of these lesions in the cerebral cortex or basal nuclei. Preliminary microscopical sections of these lesions showed that they consisted of severe necrosis of brain tissue immediately surrounding capillaries, with a halo of red cells around the necrosis.

This condition has been variously termed. It was originally called "hemorrhagic encephalitis." The current terms for it are "acute brain purpura" or "pericapillary encephalorrhagia." "Encephalitis" is a misnomer because these lesions have no inflammatory characteristics whatsoever. Postinfectious encephalomyelitis, which likewise produces perivascular myelin degeneration, is therefore ruled out by this absence of inflammatory changes. Microscopical survey of brains in cases of brain purpura discloses that although many of these lesions are hemorrhagic, not all of them are; the hemorrhagic aspect seems only to be one part of the process, and not the essential part. The hemorrhages generally look fresh, whereas the foci of necrosis in the white matter are usually accompanied by a cellular reaction of considerably older appearance. Thus, the hemorrhages may well be a terminal event in pre-

existing lesions. Closely similar lesions may be seen in cases of fat embolism involving the brain, but in that condition, both gray matter and white matter are indiscriminately affected, whereas a salient feature of the present condition is its striking confinement to the white matter.

There is nothing specific about this condition. It turns up as an incidental finding now and then in people severely ill with overwhelming sepsis. Some intoxications, particularly those due to arsphenamine, are associated with a similar picture. Once in a while, it occurs without any obvious antecedent illness.

DR. CASTLEMAN: It certainly contributed to his death.

DR. RICHARDSON: Without any doubt.

DR. LEWIS W. KANE: Was there anything in the lungs?

DR. CASTLEMAN: The lungs showed edema; the shadow noted in the lung field on the x-ray films was due to atelectasis.

DR. KANE: Were the adrenal glands abnormal?

DR. CASTLEMAN: No.

CASE 38492

PRESENTATION OF CASE

A sixty-nine-year-old farmer entered the hospital because of a mass in the neck.

One and a half years before admission the patient's wife pointed out the presence of a lump in the right side of his neck. This was firm and "fixed." He did nothing about it, however, until thirteen months before entry, when he entered another hospital for study. Although no biopsy was done, numerous x-ray films were taken, and the patient was subsequently told that nothing had been found and that he should return only if the mass changed or enlarged. Although there were no symptoms or change in size of the lesion, one month before admission the patient consulted another physician, who took a biopsy and referred him to this hospital.

The patient had been well all his life and denied having pain or any other symptoms in the neck during the period when the mass was known to be present. He had noted some hoarseness at times and more recently he found that he had to chew his food very well to prevent its catching in his throat, but he did not vomit or have any other gastrointestinal symptoms. He also thought that hearing in the right ear was reduced of late. There was no tinnitus or vertigo. The remaining systemic review was negative except for a 2-pound weight loss during the three months before entry.

Physical examination revealed a well developed and well preserved man in no apparent distress. His voice was hoarse. The left pupil was distinctly smaller than the right, but both responded to light. The oral mucosa was dry, with considerable leukoplakia especially over the palate, and the pharynx and tonsil on the right were pushed to the midline by the mass. In the right side of the neck there was a hard, firmly fixed, nontender, egg-shaped mass measuring 8 by 8 by 6 cm. (Fig. 1). It lay just posterior and a little above the sternocleidomastoid muscle over the carotid bifurcation, pushing the ear forward. In the lower portion of the right cheek there was a separate, softer, lobulated mass measuring about 2 cm. in diameter and not definitely attached to the first mass. The parotid gland was normal. The lungs were clear, and the heart was

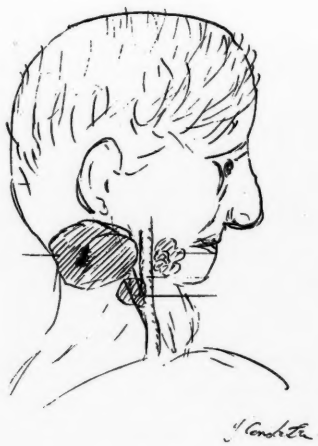


FIGURE 1.

slightly enlarged, with a Grade 2 systolic murmur in the apical and pulmonic areas. The rest of the examination was negative except for a smooth, firm prostate that was enlarged to twice the normal size.

The temperature, pulse and respirations were normal. The blood pressure was 188 systolic, 108 diastolic.

The hemoglobin was 13.4 gm. per 100 cc., and the white-cell count 6800, with 47 per cent neutrophils, 45 per cent lymphocytes, 4 per cent monocytes, 3 per cent eosinophils and 1 per cent basophils. A spinal-fluid total protein was 63 mg. per 100 cc., and the gold-sol curve was 0002210000. A roentgenogram showed the lungs to be clear. The cervical curve was reversed. There were some degenerative arthritic changes in the upper cervical spine and narrowing of a few of the intervertebral-disk spaces. There was a definite suggestion of bony rarefaction and destruction about the anterior portion of the third cervical vertebra (Fig. 2). A prevertebral soft-tissue mass measuring 6 cm. in greatest diameter just anterior to the upper cervical spine pro-

jected into the hypopharynx. No calcification was seen within the mass. A single projection of the occipital view of the skull showed no significant abnormality. A roentgenogram of the cervical spine revealed a large soft-tissue mass in the right upper neck. There was no evidence of bone destruction in the dorsal spine although some degenerative changes were present. An x-ray film of the sinuses showed thickening of the mucous membrane of the left antrum; the other sinuses were clear, and there was no evidence of bone destruction. On fluoroscopy the

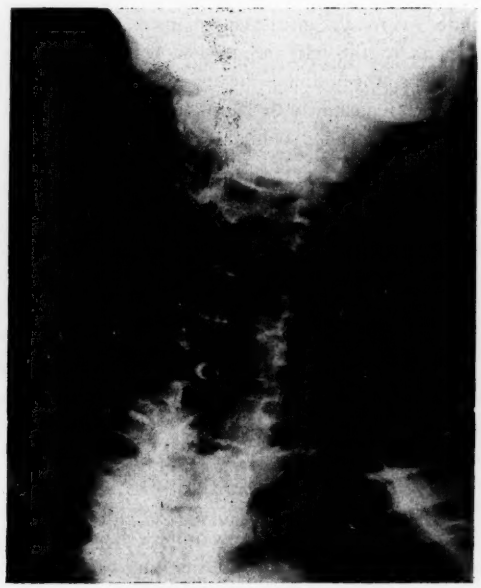


FIGURE 2. *Roentgenogram of the Cervical Spine. The arrow points to the area of bone destruction in the third and fourth cervical vertebras.*

pyriform sinus and the right side of the lower pharynx failed to fill with barium and were apparently deviated anteriorly, centered at a point posterior to the region of the hyoid bone or at the level of the tip of the epiglottis (Fig. 3). There was no definite evidence of mucosal involvement of the hypopharynx, but there was some deviation of the upper cervical esophagus at the level of the first thoracic vertebra to the right and probable, slight narrowing of the trachea in this region. A cervical myelogram showed asymmetry of the column at the level of the fourth cervical vertebra, consisting of a pressure defect on the right extending as far upward as the third cervical vertebra (Fig. 4). There was also evidence of destruction of the third and fourth cervical vertebras on the right.

On laryngoscopic examination it was difficult to visualize the vocal cords because of encroachment of tumor on the hypopharynx. The overlying mucosa was smooth and unbroken, and the epiglottis lay at rest, with the laryngeal surface in apposition with the mass. On phonation the cords could be seen and seemed to move perfectly well.

On the sixth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. BENJAMIN CASTLEMAN: This picture shows the location of the mass (Fig. 1).

DR. ERNEST M. DALAND*: That helps; because this is a lesson in anatomy, I want to emphasize its locus particularly. The tumor mass in the right side of the neck was slowly growing; it was present a year and a half before admission. The patient

FIGURE 3. *Barium-Swallow Examination. Note the distortion of the right hypopharynx in the region of the pyriform sinus.*

had not had pain and from the time he entered the first hospital to the time he was sent to this hospital, there had been no change in the size of the tumor. He had noted hoarseness. A mass in the right side of the neck and hoarseness may be due to pressure on the recurrent laryngeal nerve on that side, but this patient's vocal cords moved normally so that he did not have any paralysis of that nerve. He

*Member, Board of Consultation, and formerly, chief, Tumor Clinic, Massachusetts General Hospital.

had a small pupil on the right side, and apparently this was a rather typical Horner's syndrome due to pressure on the cervical sympathetic nerves. The oral mucosa was dry, with considerable leukoplakia over the palate. A mass as big as this pressing into the pharynx may cause traumatic changes and leukoplakia so I shall discount that.

The blood was essentially normal. The count of 45 per cent lymphocytes is somewhat high, but I think that is not important. The spinal-fluid total protein of 63 mg. per 100 cc. is distinctly high; the upper limit of normal is 40 to 45 mg. The colloidal-gold curve, I think, is not important.

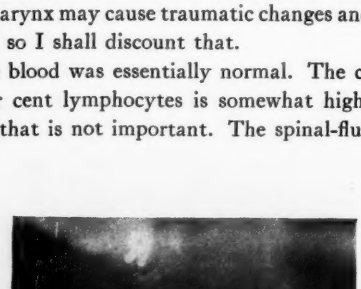


FIGURE 4. *Myelogram.*
The arrow indicates displacement of the Pantopaque in the region of the bone destruction.

The mass in the right side of the neck, 8 by 8 by 6 cm., I believe was continuous with the mass, which protruded into the pharynx because of its position and because of the way it was pressing into the pharynx. The protocol states that it lay just posterior to and a little above the sternocleidomastoid muscle and over the carotid bifurcation pushing the ear forward. I do not think the statement is quite accurate. In the drawing (Fig. 1) it is shown pushing the ear forward, and lying over and behind the sternocleidomastoid muscle, but the carotid vessels at that level are distinctly in front of the sternocleidomastoid muscle, with an inch or so between it and the carotid. The parotid gland was normal. In the x-ray films the cervical curve, which normally is upward and backward, concave from in front, was reversed, apparently owing to the pushing forward of all the organs by this large mass. There was evidence of destruction of the anterior portion of both the third and fourth cervical vertebras. On fluoroscopy the pyriform sinus on the right side of the lower pharynx failed to fill and deviated anteriorly. So the mass in the neck extended through into the pharynx, pushed the pharynx to the left and pushed the tonsil to the left over to the midline. The upper cervical esophagus also deviated slightly to the right. If that is correct, this mass extended behind the esophagus to such an extent that it had rolled the esophagus around and moved it back to the right. The mass was high up and was fixed — it could not be moved from the outside or from the inside.

May I see the x-ray films?

DR. STANLEY M. WYMAN: These first three films show reversal of the normal lordosis of the upper cervical spine. There is destruction of the anterior aspect of the body of the third cervical vertebra, and possibly this extends down as far as the fourth, involving the upper corner (Fig. 2). This involves the right lateral mass of the third cervical vertebra. This underpenetrated film demonstrates the location of the soft-tissue shadow quite well. A film from the barium-swallow examination shows the distortion and failure of filling of the right pyriform sinus in this region; according to the fluoroscopist, this portion of the pharynx was displaced anteriorly (Fig. 3). The questionable displacement of the esophagus toward the right is to be noted here at a lower point. Since this displacement is seen on only one film, I am uncertain whether this is a valid observation. I do not think I can attach any special significance to it.

In the films of the myelographic examination, the column of opaque material deviates away from the bone of the canal at about the level of the third and fourth cervical vertebras (Fig. 4). It deviates sharply to the left as if something were indenting the canal from the outside. Here, again, the bone destruction involving the third and fourth cervical vertebras is well demonstrated.

DR. DALAND: Was this a primary or a secondary tumor? If it had been a secondary tumor that had

been present for a year and a half, I think the primary tumor would have been evident. There was nothing to suggest tumor formation or abnormality in other parts of the body and no lung involvement. There was nothing that suggested any lymph-node involvement — no distant nodes and no enlarged nodes around the mass in the neck. The mass suggest a slowly growing, nonmetastasizing tumor. There was no ulceration of this mass in the mouth. The leukoplakia, I think, was secondary. There was no ulcerating, bleeding mass such as we would find if this were a primary carcinoma of the tonsil. A carcinoma of the tonsil in a year and a half certainly would have metastasized and would have broken through into the mouth, causing bleeding and ulceration and more discomfort than this patient had. A primary carcinoma would have to have started in the mucous membrane or at the base of the brain in Rathke's pouch. This is unusual and does not suggest this syndrome. I think I can rule out any primary carcinoma. Lymphosarcoma can be ruled out with the same arguments.

This could have been a mixed tumor of salivary-gland origin, which may be found anywhere around the pharynx or nasopharynx. Such tumors are slowly growing and slow to ulcerate, but they are not inclined to be as invasive as this one was. There is no calcification in this tumor as seen on the film. A long-standing mixed tumor would be quite likely to have some calcification in it.

The other possibility is a tumor of nerve origin. A neurofibroma may arise deep in the neck, may extend very slowly and does not metastasize but grows by direct extension. This tumor eroded through the vertebras. I do not visualize a neurofibroma as growing through the bone per se, but I do visualize it as eroding the cortex by pressure. I think this was a neurofibroma. I assume that, under the microscope, the pathologist had difficulty in deciding whether to call this benign or malignant. Certainly, clinically it was invasive and would destroy life; in that way it could be considered a malignant tumor, but under the microscope, it may not have had the appearance of malignancy.

Dr. Arthur S. Pier, Jr.: Could it have been a chondrosarcoma without calcification?

Dr. Daland: One would not have to see calcification. That is a possibility.

Clinical Diagnosis

?Metastatic carcinoma.
?Chordoma.

Dr. Daland's Diagnosis

Neurofibroma.

Anatomical Diagnosis

Chordoma, cervical vertebras.

Pathological Discussion

Dr. Castleman: When this patient was seen in the Tumor Clinic the physicians believed it would be easy to do an aspiration biopsy on this large protruding mass, and that was done. Microscopically, the tumor showed a great deal of mucoid stroma and connective tissue. The nuclei were dark, and the cells large. At first we thought seriously of a metastatic carcinoma, perhaps a colloid carcinoma. When I saw the patient with Dr. Schulz in the Tumor Clinic, he raised the question of a chordoma. I recalled the slide, remembered that it was not typical for carcinoma and immediately recognized it as a chordoma. This is an unusual location for a chordoma although Dr. Schulz informs me we had one in about the same place years ago.

Some years ago Dr. Roy Mabrey reviewed the cases of chordoma reported in the literature up to 1935[1] and found that 9 per cent involved the vertebras, the more common sites being the sacral region and at the base of the skull. In the vertebral cases the tumor occurred anywhere along the spinal column; there were at that time 14 cases in which the remnant of the notochord from embryonic life started to grow to produce the tumor of the notochordal cells or chordoma. Of the 14 cases, 7 were in the cervical region.

After that biopsy, the patient was then referred to the neurologic service for operation.

Dr. James C. White: Dr. Manucher Javid operated, but I saw the operation. I was surprised to hear that this was a chordoma because most of the ones we have seen have been in the sacrum; a few have been in the sphenoid. The tumor was not extremely vascular and was well encapsulated. By dividing the sternocleidomastoid muscles, Dr. Javid had a good exposure of the tumor. It was possible with finger dissection to free it from the surrounding muscles, trachea and esophagus and

to feel the attachment of the tumor to the cervical vertebras. The tumor was incised crucially, its contents were evacuated down to the bone by pituitary rongeur, and much of its capsule removed as well. I do not know how the surgeon managed to avoid the spinal accessory nerve. There was one nerve going through the tumor that was thought to be the great auricular, but the spinal accessory nerve ought to go through the sternocleidomastoid muscle and come out posteriorly near its central portion. A drain was left in for about a week. The patient was discharged from the hospital within ten days and was seen in the Tumor Clinic two weeks later. He did exceptionally well. The tumor was not completely removed; it never could be removed from the body of the cervical vertebra without collapse of the spine.

I should like to ask whether one could not rule out a neurofibroma in the preoperative diagnosis. Neurofibromas are attached to the cervical nerves; when they cause a deformity in the myelogram and raise the spinal-fluid protein, they nearly always balloon out the intervertebral foramen because the tumor compresses and erodes the pedicles — they may even erode the bodies of the cervical vertebras. There is sometimes a large, dumbbell-shaped tumor, with both intraspinal and extraspinal expansions. They produce a clear-cut pressure defect rather than a diffuse defect in the x-ray films.

Dr. Castleman: I suppose a neurofibroma in the soft tissues of the neck not connected with a spinal nerve near the vertebra may increase in size toward the vertebra and produce a similar x-ray picture.

Dr. White: When there is a rise in cerebrospinal-fluid protein, a partial block and a myelographic effect, I think there must be a dumbbell-shaped tumor.

Dr. Milford D. Schulz: I think we are sometimes led astray by the tradition that chordomas do not often appear in the neck. They are about as common there as anywhere else except for the sacral spine. Dr. Edward Sennett, who looked up the chordomas since those reviewed in 1935, found 14, of which 3 were in the cervical spine and 1 in the basisphenoid. Those in the cervical spine were in the fifth segment up. Considering the number of segments in the cervical spine, this makes the incidence fairly high; it is just as high as in the lumbar spine. Chordomas are not radiosensitive although the patient may have some respite and relief of discomfort after radiation therapy. It is hard, however, to evaluate such therapy because it always follows surgery.

Dr. Castleman: A chordoma is a benign tumor, except that as it continues to grow, it invades vertebral structures and thus causes death. If most of it is removed the patient can get along well, since it does not grow very fast.

Dr. Daland: I am chagrined that I did not make this diagnosis because in 1919 I reported the second chordoma from this hospital,[2] and it was almost a duplicate of this one. At that time 16 other cases had been reported in the literature. Ten of the reported cases had occurred at the base of the skull and one in the region of the upper cervical vertebra. Most of these have been tumors presenting in the midline and not out in the neck. The same statement is true of those occurring in the sacrum and coccyx — that is, they were midline tumors.

References

1. Mabrey, R. E. Chordoma: study of 150 cases. *Am. J. Cancer* **25**: 501-517, 1935.
2. Daland, E. M. Chordoma. *Boston M. & S. J.* **180**:571-576, 1919.

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RECORD-BREAKING HALF CENTURY

The last fifty years, as computed with the slide rule of vital statistics, have comprised man's greatest half century, at least in this and a few other countries. During this fabulous period, according to the reckoning of Dickinson and Welker,* the general mortality rate in the United States has declined from 17.2 deaths per 1000 population in 1900 to 9.6 in 1950. Concomitantly the population has doubled, and the number of persons surviving their sixty-fifth birthday has quadrupled; life expectancy at birth, estimated at forty-seven and three-tenths years in 1900 had increased to sixty-seven and six-tenths years in 1949.

*Dickinson, F. G., and Welker, E. L. Bulletin 92 of the Bureau of Medical Economic Research of the American Medical Association.

Partly as a result of this change and partly accounting for it, the leading causes of death have also undergone a striking shift in these few decades. In 1900 pneumonia caused 12.9 per cent of all deaths, with tuberculosis in second place, heart disease a close third and cancer running seventh, causing 3.6 per cent. In 1949 diseases of the heart caused 32.6 per cent of the deaths; cancer, in second place, was responsible for 13.6 per cent, and tuberculosis had dropped to seventh place with 3.0 per cent.

Some at least of these changes, in which the degenerative diseases of an aging population have supplanted those of infectious nature, may safely be attributed to improved medical care in the realm both of practice and of public health. Contributory factors are those resulting from an amelioration in the conditions of living — a more adequate food supply at all economic levels, an increasing awareness of the factors that contribute to health and longevity, better housing, and improved standards of living in general.

But Dickinson and Welker, as statisticians, are concerned in this report especially with health and longevity.

In the same half century, in this progressive country, man has also had the opportunity of developing considerable dependence on a number of devices that have tended both to improve the physical conditions under which he lives and to add complicating factors. These amenities have, it might almost be said, taken his weight from his feet and deposited it on other parts of his physical and psychologic anatomy less dynamic in their capacity for autogenous propulsion.

Rapid exogenous transit on the earth, with its multitudinous problems that affect life and limb and peace of mind; a limited conquest of the air that has defied but never seemed quite able to repeal the law of gravity; methods of communication that have robbed man of his personal privacy and almost deprived him of the capacity for reflection; entertainment in a variety of forms that have tended to sap his initiative and reduce his resourcefulness — all have contributed to the record of a half century, which, great or not, has certainly been one of mighty changes.

Other things, too, not necessarily creditable to mankind's employment of this period must become a part of the record. It has brought forth the most savage wars in history, with their tragic consequences. It has witnessed an apparently growing moral laxity accompanied by mounting juvenile delinquency, increasing crime and corruption and a loss of personal idealism and spiritual contentment. It has become to many realistic minds simply the era of the fast buck.

Something more than the prolongation of life, a social security as yet hardly tested, and an incredible increase in mechanical gadgetry are needed to justify the designation of the fifty years just past as man's greatest half century. If the hopes that have been entertained for mankind are to be realized even partly in the half century ahead, there must be higher spiritual goals for an infinitely greater segment of humanity on all continents and in all countries than at present exist. The forward listening posts of civilization must maintain a stronger contact with that "still, small voice," that it may become more audible to future generations:

> — Let sense be dumb, let flesh retire;
> Speak through the earthquake, wind and fire,
> O still, small voice of calm.

ATOMIC BOMB CASUALTY COMMISSION

With the signing of the peace treaty with Japan, a useful co-operative scientific study with Japanese colleagues in medicine and genetics is brought to attention. The Atomic Bomb Casualty Commission, managed by the National Academy of Sciences under contract with the Atomic Energy Commission, is an outgrowth of early joint efforts by the Japanese and American medical professions to learn the effects of this new and terrible weapon on the human body.

The initial studies were made by the staffs of several of the Japanese medical schools jointly with medical personnel of the United States Navy, of the Army Medical Corps and of the Manhattan Engineering District, and it is fitting that this joint enterprise should continue, so that the long-range somatic and hereditary effects can be determined.

It is also a tribute to American sympathy for human suffering that one of the earliest activities of the occupation forces in Japan was the careful study of the survivors of the Hiroshima and Nagasaki bombings and the instruction by American physicians of their Japanese colleagues in all the advances in medicine that had been made in this country during the war. Thus, many of the injured survived who would otherwise have died.

The wise policy of the occupation authorities that Allied personnel should not treat Japanese nationals prevented misunderstandings because of language and other difficulties and made a far more lasting contribution than any immediate therapeutic help might have given, in that the doctors of Japan learned at first-hand how to apply the most up-to-date scientific medical advances for the benefit of their fellow citizens.

With the signing of the peace treaty the work of the Atomic Bomb Casualty Commission is continuing, the Department of State and the Department of Defense having actively supported it. Not only have Japanese scientists co-operated by participating in this international effort supported by the Atomic Energy Commission but also the Japanese government has recognized the importance of the work and its significance, so that today, under the direction of Dr. Grant Taylor, nearly 100 Americans and several times that many Japanese are concentrating on learning the utmost from the survivors and are setting a splendid example of international scientific co-operation.

The Atomic Bomb Casualty Commission has available one of the best equipped medical libraries and medical laboratories in Japan and not only is using them effectively in its own work but also is using them as a means of aiding its Japanese colleagues to keep abreast of the progress being made so rapidly throughout the free world.

There are those who believe that the atomic bombs should not have been used on Hiroshima and Nagasaki. Two extenuating facts must be borne in mind, however: the war was started by Japan at Pearl Harbor, and the use of the atomic bombs brought an end to the war without invasion of Japan. Only those with knowledge of the plans of this invasion and only those familiar with the bravery of the Japanese in even a hopeless cause can understand the literally millions of Japanese lives and the

hundreds of thousands of American lives that were spared by a decision that rendered this invasion unnecessary. The military leaders of Japan could not surrender to conventional weapons without losing face. There was no dishonor in surrendering to a nation possessing a weapon of cataclysmic force.

Japanese and American doctors have been working together at Hiroshima and Nagasaki for seven years. Much good has come of this. May this cooperation long continue!

GREATER BOSTON SCHOOLS OF NURSING

THE Nursing Council of United Community Services of Greater Boston is providing a distinct community service of its own, in these days of nurse shortages, in the preparation and publication of a descriptive catalogue of the schools of nursing in the area.

All the institutions listed have the approval of the Massachusetts Approving Authority for Schools of Nursing, which makes their graduates eligible to take the qualifying examinations to enable them to practice as registered nurses or as registered attendant nurses in Massachusetts; some of them, in addition, are accredited or have received temporary accreditation by the National Nursing Accreditation Service.

Comprising the list are 22 schools offering three-year diploma programs in nursing, 5 schools offering programs in attendant nursing and 5 schools offering collegiate programs.

The nursing sorority of Boston has long taken pride in the fact that here was founded the first school of nursing in the country, and from it the country's first trained nurse was graduated. It can take equal pride in the continued maintenance of the high standards of nursing education that were then established.

"DAMSEL ARISE"

ELSEWHERE in this issue of the *Journal* a letter from the director of Crittenton Hastings House appears, reminding physicians of this area that two old and respected institutions have recently merged their resources.

The Florence Crittenton Home and Hospital, for unmarried mothers, was literally one of a chain of such institutions, organized under that name many years ago by a philanthropic citizen; the links in the chain were each supported, at least in part, by a group of local "circles," industriously working in its behalf.

Hastings House, serving in Boston a similar purpose, was originally established and long and favorably known under the name Talitha Cumi — "Damsel, Arise." Because of the similar nature of their services and the abundance of charitable organizations existing in Greater Boston, many of them with identical or overlapping functions, Hastings House and the Florence Crittenton Home and Hospital were persuaded by United Community Services to combine their facilities.

Recognizing no restrictions on account of "race, color, creed or place of residence," Crittenton Hastings House stands ready to serve those who can make best use of the unique services offered.

Eruptions of the skin on small children, of a singular character, have been recognized by physicians at the North, the present autumn, that do not yield very readily to medication.

Boston M. & S. J., *December 8, 1852*

BY THE LONDON POST

AN AMERICAN IN LONDON

A Canadian doctor once remarked to me that, in many respects, Canadians regard themselves as occupying a position midway between the English and the Americans. He said he thought the situation was well illustrated by the time hospital-ward work is started in the respective countries. "In America" he said, "they start their ward rounds at 8 o'clock, in England you start at 10 o'clock — but in Canada we start at 9 o'clock!"

With this in mind and with some slight experience of the 8 o'clock American ward round, I asked an American friend at present on fellowship at a large London hospital how he was reacting to our mode of life. I am glad to say that he was enthusiastic — in nearly all respects. He had seen the bedside approach of the British clinicians of which he had heard, but was relieved to find that we do rely upon a battery of special investigations to help in diagnosis in the same way as on the other side. He had noticed the reverence with which juniors regard their seniors—but again was relieved to

find that outside the ward or clinic, the senior man will talk to the middle man and the middle man will talk to the junior man.

He had found, however, that although our surgeons are as keen on early postoperative ambulation as those in the United States, this does not apply to the obstetric service, where he had had first hand experience, for his wife had honored Britain by being delivered of her second born by our National Health Service. Strict bed rest for the parturient mother is still insisted upon. Ostensibly, this is because more importance is laid upon obtaining rapid involution of the uterus than upon the danger of venous thrombosis, but my friend suspected that there is a more subtle reason: he believes that we British doctors are more subservient to our nursing colleagues than we care to admit. The ward sister (head nurse) carries a great tradition of authority, dictating ward rules for the discipline of patients and establishing a ward routine to which all, including the doctors, must conform. So much obstetrics having been in the sole charge of midwives in the past, it is perhaps not surprising that in the obstetric ward the rigid traditions of the past are the hardest to break. Furthermore, in these traditions my friend had found the answer to our 10 o'clock ward rounds: the ward sister will not let us in any earlier.

The Nuffield Foundation

Lord Nuffield once said that success in life is rarely due to good fortune alone and that more often it results from the recognition and exploitation of every opportunity which presents. No doubt in these words he was reflecting his own experience, for to have developed the vast Nuffield Motor Company from a small bicycle business in Oxford must have required a constant watch for new opportunities. Doubtless, too, it was the atmosphere of this university city, with its cosmopolitan hordes of pedaling undergraduates, that inspired him to establish the Nuffield Foundation when his own success enabled him to do so.

Like that of Rockefeller, his main aim was to promote the welfare of mankind and in his gift of £10,000,000 he provided the Foundation with its main source of income. In the seventh annual report the achievements of the past year, which is the third in a current five-year program, have been summarized. In this period grants have been made to assist research into problems in widely separated fields. Biologic, sociologic and other scientific projects have been sponsored both in the United Kingdom and in other parts of the Commonwealth.

In particular, a grant of £60,000 was allocated to the National Corporation for the care of old people, a body that was set up to encourage voluntary organizations to help the aged. A further sum was set aside for research into the process of aging — a problem that has attracted universal attention in view of the increase in length of the average life span made possible by recent advances in medical science. Other sociologic research projects that have been encouraged include a study at Edinburgh University of the cultural and social habits of colored people and the relation between colored and white people in the United Kingdom.

At Bedford College, London, a research fellowship has been established to review the whole field of social research. There, all the problems of social deviation, including crime and other forms of social failure, will be considered. Another interesting project is underway at Oxford University, where a national survey into personal savings and saving habits is being undertaken.

When the Government found itself unable for financial reasons to offer sufficient support for Manchester University to embark upon building the world's largest steerable radio telescope, the Nuffield Foundation offered to share the cost so that the work could begin this summer. Accordingly the Foundation has promised £200,000 toward a probable total cost of £400,000.

The report recognizes in the increasing proportions of university incomes that are being derived from central-government funds a possible threat to the traditional independence that is essential to academic work. It suggests, however, that private trusts such as the Nuffield Foundation, by providing alternative sources of financial support, can do much to offset this danger.

International Congress of Internal Medicine

The second International Congress of Internal Medicine, attended by representatives from 30 countries, was held in London from September 15 to 18. At the opening meeting Sir Russell Brain, president of the Congress and president of the Royal College of Physicians, attempted to define internal medicine. He said that the difference between the specialist and the internist was that the former tends to regard a part of the patient from his own point of view whereas the latter considers the whole patient from every aspect.

At each of the four scientific sessions one broad subject was considered in symposium form. The subjects chosen were the sprue syndrome, disturbances of fluid and electrolyte balance, the neurotropic viruses and antibiotics in man. On each occasion the sessions opened with papers by leading authorities and concluded with an opportunity for open discussion. By limitation of the number of problems considered it was possible to regard the subjects from every point of view and thus to answer the President's plea for thoroughness on the part of the internist.

The social functions included a dinner at the Mansion House by invitation of the Lord Mayor.

Speaking at this dinner, Lord Moran said that no visit to London was complete unless the visitor dined with the Lord Mayor. In response, Sir Leslie Boyce, the present Lord Mayor, who was born and bred in Australia, claimed that London was still going strong even if once in a thousand years it had to send to the other end of the world to find a Lord Mayor.

JOHN LISTER, M.D.

CORRESPONDENCE

CRITTENTON HASTINGS HOUSE

To the Editor: I am writing to you because I believe the readers of the *Journal* will be interested in the facilities offered by Crittenton Hastings House for unmarried mothers.

Physicians are often asked to make plans for the care of the unmarried mother. The patient herself and her relatives and friends, as well as the community at large, place their confidence in him and his ability to inform them about resources of help.

Crittenton Hastings House, the present name for the merged services of the Florence Crittenton Home and Hastings House, (previously Talitha Cumi) is a Red Feather agency, organized and operated to help the unmarried mother in her time of greatest need. It provides temporary sanctuary from the community in which the patient lives, good medical care and professionally trained counsellors to assist in making plans for the future of mother and baby.

The unmarried mother who seeks such services can best benefit by entering the home several months before the date of expected confinement and remaining at least a month after delivery. Doctors who are considering referral of such patients will appreciate the emphasis on this minimum period as necessary to the maintenance of the best standards of medical care. They will also understand that the complex emotional and social factors involved in the problem of extramarital pregnancies must have adequate time for study and evaluation. To this end, Crittenton Hastings House offers the skill of professionally trained social workers, with the help of a consulting psychiatrist and, as needed, a clinical psychologist.

At present, deliveries take place at the Boston Lying-in Hospital, where the mother remains a brief period and from which she returns to Crittenton Hastings House, where she receives bedside care from registered nurses. Weekly clinics under the supervision of doctors from the Lying-in Hospital protect the health of the prenatal or post-partum patient, and the babies receive equally regular examination by members of the Pediatrics Department of the Massachusetts General Hospital. Diets and general regimens prescribed are carefully followed by the nurses and dietitian.

Light housework duties, consistent with the patient's condition, are part of the program, which also includes daily rest periods, recreation, hours of visiting with relatives and friends, and religious services, either in the home or in the church of the patient's choice. Plans for the future are directed toward an extension of the arts and crafts, and group therapy. At present, as an adjunct to individual counselling the patients work out many of their common problems through a democratically organized council.

Rates are adjusted to ability to pay, and no one is refused admission because of lack of funds.

Although there are no restrictions of race, color, creed or place of residence, it is essential for the doctor referring a patient to consider her potential capacity to make use of the multiple services offered and to become integrated in the group of 35 or more patients. For this reason, the severely disturbed or the mentally retarded cannot be considered for admission.

Inquiries to clarify the services mentioned above, or to answer uncovered aspects of the services offered by this home for unmarried mothers, will be welcome. Physicians are cordially invited to visit Crittenton Hastings House to become better acquainted with its facilities. Arrangements for such a visit may be made with the director, Mrs. Louise T. Graves, Crittenton Hastings House, 10 Perthshire Road, Brighton 35, Massachusetts. (Telephone, STadium 2-7600.)

LOUISE T. GRAVES
Director

Crittenton Hastings House
10 Perthshire Road
Brighton 35, Massachusetts

NONCLINICAL NOTES

APPOINTMENT OF DR. CHILD

The appointment of Dr. Charles G. Child, III, of New York City, as surgeon-in-chief of the Pratt Diagnostic Clinic — New England Center Hospital and as professor of surgery at Tufts College Medical School has been announced.

Dr. Child, who is associate professor of clinical surgery at Cornell University Medical College and attending surgeon at the New York Hospital, will begin his new duties in January.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Military Standard Marking of Shipments. Issued by the Armed Services Medical Procurement Agency. 4°, paper, 49 pp., with 19 illustrations. Washington: United States Government Printing Office, 1951. 35 cents.

This manual is essential to all persons and organizations concerned with the military establishment of the Government.

Problems of Consciousness: Transactions of the Second Conference, March 19–20, 1951, New York, New York. Edited by Harold A. Abramson, M.D., department of physiology, College of Physicians and Surgeons, Columbia University. 8°, cloth, 178 pp., New York: Josiah Macy, Jr., Foundation, 1951. $3.25.

Three subjects were discussed at this second conference: a psychopathological and psychodynamic view of consciousness; variations in the scope of awareness; and variations in the scope of awareness in schizophrenic patients.

Rheumatic Diseases, Based on the Proceedings of the Seventh International Congress on Rheumatic Diseases: Prepared by the Committee on Publications of the American Rheumatism Association. Charles H. Slocumb, M.D., chairman. 8°, cloth, 449 pp., with 126 illustrations and 63 tables. Philadelphia: W. B. Saunders Company, 1952. $12.00.

The Congress on Rheumatic Diseases was participated in by nearly two hundred specialists from all over the world. The papers have been assembled into sections by subjects, too numerous to enumerate, but covering the whole field of rheumatic diseases and allied disorders. There is a comprehensive index of subjects and also one of authors, and the publishing is excellent. The book is recommended for all medical libraries and to all persons interested in the subject.

Biological Antioxidants: Transactions of the Fifth Conference, November 30–December 1, 1950, New York, New York. Edited by Cosmo G. Mackenzie, Department of Biochemistry, University of Colorado School of Medicine. 8°, paper, 229 pp., with illustrations and tables. New York: Josiah Macy, Jr., Foundation, 1951. $3.75.

This conference was devoted to radiation and irradiation and their effects, perioxides and mutations, and free radicals, perioxides and antioxidants in some biologic processes.

Probleme der Schutzimpfung und die Bekämpfung der Rindertuberkulose. By Prof. Dr. G. Ramon, director, internationalen Tierseuchenamtes, and honorary director, Pasteur Institute in Paris. Translated into German by G. Fluckiger, director, eidgenössischen Veterinäramtes and professor, Universität Bern. 8°, paper, 52 pp. Stuttgart: Georg Thieme, 1952. DM 7.20. Distributed by Grune and Stratton, New York.

This monograph discusses preventive inoculation and control of tuberculosis in cattle. The text is divided into two parts: immunity and allergy in tuberculosis, and the control of cattle tuberculosis.

Cybernetics: Circular Causal and Feedback Mechanisms in Biological and Social Systems: Transactions of the Eighth Conference, March 15-16, 1951, New York, New York. Edited by Heinz von Foerster, Department of Electrical Engineering, University of Illinois, Champaign, Illinois. Assistant editors, Margaret Mead, American Museum of Natural History, New York, and Hans L. Teuber, Department of Neurology, New York University College of Medicine. 8°, cloth, 240 pp. New York: Josiah Macy, Jr., Foundation, 1952. $4.00.

This volume contains six papers and an appendix. They comprise four articles on communication patterns in problem-solving groups; communication between men; meaning of language; between sane and insane: hypnosis; and between animals. Two other papers discuss a maze-solving machine and basic symbols. There is a valuable presentation of the nomenclature of information theory by Donald M. MacKay, first read in London at a symposium in September 1950, and revised in April 1951.

NOTICES

ANNOUNCEMENT

Dr. Milton M. Sisson announces the removal of his office from 31 Federal Street to 474 Main Street, Greenfield.

NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

A meeting of the New England Society of Physical Medicine will be held in the amphitheater of the Children's Hospital, Boston, on Wednesday, December 10, at 8 p.m.

PROGRAM

The Management of the Patient with Acute Poliomye'itis. William T. Green, M.D., and staff.

All members of the medical profession are cordially invited.

NEW ENGLAND CENTER HOSPITAL HOUSE OFFICERS' ASSOCIATION

A meeting of the House Officers' Association of New England Center Hospital will be held in the Stearns Auditorium of New England Center Hospital on Friday, December 12, at 7 p.m.

Dr. Claude S. Beck, professor of cardiovascular surgery, Western Reserve University School of Medicine, will speak on the subject "Arterialization of the Coronary Sinus for Coronary-Artery Disease."

All interested persons are invited to attend.

SPRINGFIELD ACADEMY OF MEDICINE

Meetings of the Springfield Academy of Medicine will be held on December 9 and January 13. Speakers will be respectively, Drs. J. C. Nemiah and J. Roswell Gallagher, of Boston.

AMERICAN DIABETES ASSOCIATION PRIZE

The American Diabetes Association offers a $250 prize to medical students and interns for a paper on any subject relating to diabetes. The paper can be a report of original studies, a biographic or historical note, a case report with suitable comment or a review of the literature.

Manuscripts must be submitted on or before April 1, 1953, to the editorial offices of *Diabetes*, the journal of the American Diabetes Association, 11 West 42nd Street, New York 36, New York.

The award of $250 has been made possible through the generosity of the St. Louis Diabetes Association, an affiliate of the American Diabetes Association.

SOUTHERN SURGICAL ASSOCIATION

The sixty-fourth annual session of the Southern Surgical Association will be held at the Hollywood Beach Hotel, Hollywood, Florida, December 9-11.

DAVID ANDERSON-BERRY PRIZE

A David Anderson-Berry Silver-Gilt Medal, together with a sum of money amounting to about £100, will be awarded during 1953 by the Royal Society of Edinburgh to the person who, in the opinion of the Council, has recently produced the best work on the therapeutic effect of x-rays on human diseases. Applications, which may be based on both published and unpublished work and should be accompanied by copies of the relevant papers, must be in the hands of the General Secretary, Royal Society of Edinburgh, 22 George Street, Edinburgh, 2, *not later than March 31, 1953.*

SOCIETY MEETINGS AND CONFERENCES

OCTOBER 6–DECEMBER 8 AND MARCH 2–MAY 4. Massachusetts Department of Mental Health. Postgraduate Seminar in Neurology and Psychiatry. Page 540, issue of October 2.

OCTOBER 7–December 9. Massachusetts Department of Mental Health. Course in Child Psychiatry (Pediatric Neuropsychiatry). Page 540, issue of October 2.

DECEMBER 5. New England Center Hospital House Officers' Association. Page 868, issue of November 27.

DECEMBER 5–JANUARY 30. Combined Anesthesia Teaching Conferences of Boston. Page 785, issue of November 13.

DECEMBER 6–11. American Academy of Dermatology and Syphilology. Page 828, issue of November 20.

DECEMBER 6–22. Springfield Hospital Educational Program. Page 827, issue of November 20.

DECEMBER 6–JUNE 2. Mount Auburn Hospital Panel Discussions. Page 868, issue of November 27.

DECEMBER 8. Boston Society of Biologists. Page 868, issue of November 27.

DECEMBER 9. Harvard Medical Society and Boston City Hospital House Officers' Association. Page 868, issue of November 27.

DECEMBER 9. New York Society for Circulatory Diseases. Page 827, issue of November 20.

DECEMBER 9–11. Southern Surgical Association. Notice above.

DECEMBER 9 and January 13. Springfield Academy of Medicine. Notice above.

DECEMBER 10. New England Society of Physical Medicine. Notice above.

DECEMBER 10. Greater Boston Medical Society. Page 868, issue of November 27.

DECEMBER 10. New England Pediatric Society. Page 826, issue of November 20.

DECEMBER 10–13. New York State Society of Anesthesiologists. Page 744, issue of November 6.

DECEMBER 10–17. Lahey Clinic Lectures. Page 698, issue of October 30.

DECEMBER 10–APRIL 8. Postgraduate Medical Institute. Page 452, issue of September 18.

DECEMBER 12. New England Center Hospital House Officers' Association. Notice above.

DECEMBER 12 AND 13. Association for Research in Nervous and Mental Disease. Page 583, issue of October 9.

DECEMBER 15–17. American Academy of Obstetrics and Gynecology. Page 744, issue of November 6.

DECEMBER 15–MARCH 23. Postgraduate Course in General Medicine. Page 697, issue of October 30.

JANUARY 14. Essex North District Medical Society. Page 743, issue of November 6.

FEBRUARY 6. New England Society of Anesthesiologists. Page 827, issue of November 20.

FEBRUARY 9 AND 10. Annual Congress on Medical Education and Licensure. Page 786, issue of November 13.

MARCH 2–5. New Orleans Graduate Medical Assembly. Page 828, issue of November 20.

APRIL 3. New England Society of Anesthesiologists. Page 418, issue of September 11.

APRIL 29 AND OCTOBER 28. New England Obstetrical and Gynecological Society. Page 868, issue of November 27.

(*Notices concluded on page xv*)